# GBA Gene

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Glucosylceramidase beta

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## 1. Normal Function

The *GBA* gene provides instructions for making an enzyme called beta-glucocerebrosidase. This enzyme is active in lysosomes, which are structures inside cells that act as recycling centers. Lysosomes use digestive enzymes to break down toxic substances, digest bacteria that invade the cell, and recycle worn-out cell components. Based on these functions, enzymes in the lysosome are sometimes called housekeeping enzymes. Beta-glucocerebrosidase is a housekeeping enzyme that helps break down a large molecule called glucocerebroside into a sugar (glucose) and a simpler fat molecule (ceramide). Glucocerebroside is a component of the membrane that surrounds cells. It gets broken down by beta-glucocerebrosidase when cells die, and the components are reused as new cells are formed.

## 2. Health Conditions Related to Genetic Changes

### 2.1 Parkinson Disease

Changes in the *GBA* gene are also associated with Parkinson disease and parkinsonism, which are similar disorders that affect movement. Characteristic features include tremors and impaired balance and coordination (postural instability). People with Gaucher disease (described above) have mutations in both copies of the *GBA* gene in each cell, while those with a mutation in just one copy of the gene are called carriers. People with Gaucher disease and people who are carriers of a *GBA* gene mutation have an increased risk of developing Parkinson disease or parkinsonism.

Symptoms of Parkinson disease and parkinsonism result from the loss of nerve cells (neurons) that produce dopamine. Dopamine is a chemical messenger that transmits signals within the brain to produce smooth physical movements. It remains unclear how *GBA* gene mutations are related to these disorders. Studies suggest that changes in this gene may contribute to the faulty breakdown of toxic substances in neurons by impairing the function of lysosomes. Alternatively, the changes may increase the formation of abnormal protein deposits. As a result, toxic substances or protein deposits could accumulate and kill dopamine-producing neurons, leading to abnormal movements and balance problems.

### 2.2 Gaucher Disease

More than 380 mutations in the *GBA* gene have been identified in people with Gaucher disease, a disorder with varied features that affect many parts of the body. Affected individuals can have enlargement of the liver and spleen (hepatosplenomegaly), blood cell abnormalities, and rarely, severe neurological problems. The mutations occur in both copies of the gene in each cell. Most of the *GBA* gene mutations responsible for Gaucher disease change single protein building blocks (amino acids) in beta-glucocerebrosidase, altering the structure of the enzyme and preventing it from working normally. Other mutations delete or insert genetic material in the *GBA* gene or lead to the production of an abnormally short, nonfunctional version of the enzyme.

Mutations in the *GBA* gene greatly reduce or eliminate the activity of beta-glucocerebrosidase in cells. As a result, glucocerebroside is not broken down properly. This molecule and related substances can build up in white blood cells called macrophages in the spleen, liver, bone marrow, and other organs. The abnormal accumulation and storage of these substances damages tissues and organs, causing the characteristic features of Gaucher disease.

### 2.3 Dementia with Lewy Bodies

*GBA* gene mutations can increase the risk of developing dementia with Lewy bodies; however, some people with a mutation in the *GBA* gene never develop this condition. Dementia with Lewy bodies is characterized by intellectual decline (dementia); visual hallucinations; sudden changes in attention and mood; and movement problems characteristic of Parkinson disease (described above) such as rigidity of limbs, tremors, and impaired balance and coordination.

Mutations in one copy of the *GBA* gene increase the risk of developing dementia with Lewy bodies. These mutations result in the production of an altered beta-glucocerebrosidase enzyme. This abnormal enzyme may interfere with the function of lysosomes and the normal breakdown of a protein called alpha-synuclein, which increases the risk that these proteins accumulate and form Lewy bodies. Accumulation of these protein clusters throughout the brain impairs neuron function and ultimately causes cell death. Over time, the loss of neurons increasingly impairs intellectual and motor function and the regulation of emotions, resulting in the signs and symptoms of dementia with Lewy bodies.

## 3. Other Names for This Gene

- acid beta-glucosidase
- algucerase
- beta-D-glucosyl-N-acylsphingosine glucohydrolase
- beta-glucocerebrosidase
- GBA1
- GLCM_HUMAN
- GLUC
- glucocerebrosidase
- glucocerebroside beta-glucosidase
- glucosidase, beta, acid
- glucosidase, beta; acid (includes glucosylceramidase)
- glucosphingosine glucosylhydrolase
- glucosylceramide beta-glucosidase
- imiglucerase

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