# GBA gene

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 when cells die and recycled as new cells are formed.

---

Variants in GBA are the most common genetic risk factor for Parkinson's disease (PD), and are especially prevalent in the Ashkenazi Jewish (AJ) population. However, most studies on GBA in AJ genotype only seven selected Gaucher-associated pathogenic variants rather than sequencing the whole gene, which may leave carriers of PD-associated GBA variants undiscovered.

METHODS: GBA was fully sequenced using molecular inversion probes (MIPs) and Sanger sequencing in 735 AJ PD patients and 662 AJ controls, from Israel and New York. Additional AJ control data (n = 3044) from the Inflammatory Bowel Disease Exome Portal was used.

RESULTS: Full GBA sequencing increased the number of variants discovered by 17.4%, compared to targeted genotyping. An additional 17 PD patients were identified with GBA-associated PD. The p.E326K variant was found in 1.6% of AJ PD patients, making it the second most common PD-associated GBA variant in AJ. GBA variants were found in 18% of PD patients and 7.5% of controls (OR = 2.7, 95%CI = 1.9-3.8, p < 0.0001).

CONCLUSION: Without full sequencing of GBA, or at minimum including p.E326K in the genotyping panel, a significant proportion of variant carriers go undiscovered and may be incorrectly assigned as non-carriers in studies or clinical trials [1)].

1)
Ruskey JA, Greenbaum L, Roncière L, Alam A, Spiegelman D, Liong C, Levy OA, Waters C, Fahn S, Marder KS, Chung W, Yahalom G, Israeli-Korn S, Livneh V, Fay-Karmon T, Alcalay RN, Hassin-Baer S, Gan-Or Z. Increased yield of full GBA sequencing in Ashkenazi Jews with Parkinson's disease. Eur J Med Genet. 2018 May 26. pii: S1769-7212(18)30124-1. doi: 10.1016/j.ejmg.2018.05.005. [Epub ahead of print] PubMed PMID: 29842932.