Explore a Trait Assignment – Parkinson’s Disease

1. After reading the "23AndMe Facts on Parkinson’s Disease" provided below, write a one-paragraph summary in your own words of the information provided. Include answers to the following questions:
   - What is the difference between preliminary research and established research?
   - How likely is Parkinson’s Disease to be inherited?
   - What are the mutations that are currently tested for by 23AndMe for Parkinson’s Disease?
   - If someone tested positive for one of these mutations, describe his increased risk for developing Parkinson’s Disease?
   - What is the likelihood of developing Parkinson’s Disease if you test positive for these mutations?

2. Several research studies are referenced after the “23AndMe Facts on Parkinson’s Disease” please summarize what is found in one of these research studies including a decision about how it would influence someone’s decision to be tested.

3. Considering ethnic background, find a source that provides information tested in ethnicity.

23AndMe Facts on Parkinson’s Disease

Parkinson’s Disease

Parkinson’s disease is a disorder of the brain’s motor system caused by a loss of dopamine-producing brain cells. Approximately one and a half million Americans have the disease, and about 50,000 new patients are diagnosed each year. The main symptoms are trembling in the hands, arms, legs, jaw, and face; stiffness of the limbs and trunk; slowed movement; and impaired balance and coordination. Symptoms of Parkinson’s disease usually come on gradually and affect people over the age of 50, although there are rare forms that progress more quickly and strike at a younger age. Though very little is known about the genetics of Parkinson’s, mutations in a gene known as LRRK2 have been found to greatly increase a person’s likelihood of developing the condition.

The following results are based on Established Research for 10 reported markers, updated April 26th, 2012.

Genes vs. Environment

27 % Attributable to Genetics

The heritability of Parkinson’s is relatively low but a recent study estimated it to be about 27% in European populations. This means that environment generally plays a larger role than genetics in determining a person’s risk for the disease. However, a small fraction of Parkinson’s cases are attributed to rare mutations in a small number of genes, including the G2019S mutation in LRRK2, which is included in this report. People with the LRRK2 G2019S mutation have a much higher than average risk of developing Parkinson’s disease during their lifetimes. This report also discusses other genetic factors that are associated with higher risk for PD in European and Asian populations.

Gene or region: LRRK2

SNP: rs34637584

Mutations in the LRRK2 gene are one of the most common known genetic causes of Parkinson’s disease (PD).

More than 50 variants are known in the LRRK2 gene. Several of these have been associated with PD. This variant reported by 23andMe, rs34637584, also known as the G2019S mutation, is the best-studied LRRK2 SNP related to Parkinson’s in individuals with European ancestry.

Parkinson’s is a fairly rare disease. The average person has a 1-2% chance of developing the disease during his or her lifetime. The chance that a person with the G2019S mutation will develop Parkinson’s is much higher than average and increases with age. One recent study found that people with the G2019S mutation have a 28% chance of developing Parkinson’s by the age of 59, 51% by the age of 69 and 74% by the age of 79. However, estimates of PD risk due to the G2019S mutation vary greatly. While it is well established that the mutation’s effect is very strong, there is no consensus about its exact magnitude.

Of all people with Parkinson’s, few have the G2019S mutation, but it is present at high levels in patients from some ethnic groups. Up to 40% of people with PD who are of Arab-Berber ancestry and 20% of Ashkenazi Jewish people with PD have this mutation.

Scientists do not know why only some people with the G2019S mutation get PD. There may be unknown effects due to other genes or environmental factors.

Citations

**Gene or region: LRRK2**

**SNP: rs34778348**

Mutations in the LRRK2 gene are one of the most common known genetic factors associated with Parkinson's disease (PD). The G2385R LRRK2 mutation, identified here as the SNP rs34778348, has been identified in about 5-10% of sporadic Parkinson's cases in Asian populations. Multiple studies in Chinese, Japanese, and Korean populations have established that the A version of the SNP is associated with about three times increased risk for PD.

While the G2019S mutation (identified here as rs34637584), is the best-studied LRRK2 SNP related to PD in European, Ashkenazi Jewish, and some northern African populations, it is not found in Asian populations. Instead, the G2385R mutation in LRRK2, which is rare or not present in populations with European ancestry, appears to confer susceptibility to PD in Asian populations.

Parkinson's disease is very rare and environmental factors also play a large role in whether someone develops the disease. Individuals with Asian ancestry who have the G2385R mutation are at increased risk of developing PD, but only some with the mutation will actually develop it and most Asian individuals with PD do not have this mutation.

**Citations**


*Mov. Disord.* 24(7):1034-41.


**Gene or region: GBA**

**SNP: i4000415**

This variant is in the GBA gene, which encodes a protein called glucosylceramidase. Numerous studies have now shown that those with a single copy of a GBA mutation may be at increased risk of developing Parkinson's disease.

There is also evidence that people with GBA mutations may develop Parkinson's at an earlier age than people without GBA mutations. Research suggests that reduced glucosylceramidase activity caused by mutations in GBA may increase cell sensitivity to toxins, but additional studies are needed to elucidate these mechanisms.

The GBA variant that 23andMe reports corresponds to the N370S mutation, the most common GBA mutation found in Ashkenazi Jewish individuals. A large, multi-center study observed that about 14% of Ashkenazi Jewish individuals with Parkinson's disease had the N370S mutation. N370S is relatively less common in non-Ashkenazi populations, and GBA mutations as a whole appear to account for a smaller percentage of Parkinson's disease in non-Ashkenazi populations. Mutations in GBA also cause a rare, recessive genetic condition called Gaucher's disease that is especially common in the Ashkenazi Jewish population.

Parkinson's disease is very rare and environmental factors also play a large role in whether someone develops the disease. The N370S mutation is associated with about four times increased risk for PD. The N370S mutation has not been observed in Asian populations, and has not been studied in populations with African ancestry.

**Citations**


**Gene or region: SNCA**

**SNP: rs356220**

This SNP is located near the SNCA gene, which encodes a protein called α-synuclein. Rare mutations in this gene were previously found to cause familial forms of Parkinson's disease. Researchers aren't yet sure how common variants in SNCA increase susceptibility to Parkinson's, but preliminary evidence suggests that the mechanism may have something to do with increased levels of the protein.

Multiple studies have established an association between this SNP and Parkinson's disease in both European and Asian populations. In Europeans, the less common T version of the SNP is associated with slightly increased risk for Parkinson's disease. In Asians, the T version is slightly more common, and so the C version is considered slightly protective against PD. The association has not been studied in populations with African ancestry.
Citations


Gene or region: MAPT

SNP: rs393152

This SNP is located near the MAPT gene, which encodes a protein called microtubule-associated protein tau, a major component of neurons. Variants in MAPT have already been associated with other neurodegenerative disorders as well as with familial forms of Parkinson's disease.

Multiple studies have identified an association between this SNP and Parkinson's disease in populations with European ancestry. In Europeans, the G version of the SNP is associated with slightly decreased risk for Parkinson's disease. A different SNP in the PARK16 region is associated with slightly decreased risk for Parkinson's disease. A different SNP in the PARK16 region is associated with slightly decreased risk for Parkinson's disease in Asians. SNPs in the PARK16 region have not been studied in populations with African ancestry.

Citations


Gene or region: PARK16

SNP: rs947211

Numerous SNPs in a region of chromosome 1 (1q32) called PARK16 have been associated with Parkinson's disease. The PARK16 region contains several genes. The reported SNP is located between the SLC41A1 and RAB7L1 genes and could affect either of these neighboring genes. It might also have been discovered because it serves as a signpost for a nearby, unidentified genetic factor that is related to Parkinson's disease.

A large meta-analysis study consisting of about 16,000 people with Parkinson's disease and nearly 50,000 without the disease identified an association between this SNP and Parkinson's disease. In individuals with European ancestry, the A version of the SNP is associated with slightly decreased risk for Parkinson's disease. A different SNP in the PARK16 region is associated with slightly decreased risk for Parkinson's disease in Asians. SNPs in the PARK16 region have not been studied in populations with African ancestry.

Citations


Gene or region: PARK16

SNP: rs823156

Numerous SNPs in a region of chromosome 1 (1q32) called PARK16 have been associated with Parkinson's disease. The PARK16 region contains several genes. The reported SNP is in the SLC41A1 gene, which encodes a protein that transports magnesium out of cells and sodium into cells. More research is needed to understand its potential involvement in Parkinson's disease. Alternatively, this SNP might have also been discovered because it serves as a signpost for a nearby, unidentified genetic factor that is related to Parkinson's disease.

Multiple studies have identified an association between this SNP and Parkinson's disease in populations with Asian ancestry. In Asians, the G version of the SNP is associated with slightly decreased risk for Parkinson's disease. A different SNP near the SLC41A1 gene is associated with slightly decreased risk for Parkinson's disease in Europeans. SNPs in the PARK16 region have not been studied in populations with African ancestry.

Citations

Parkinson's Disease: Preliminary Research

Parkinson's disease is a disorder of the brain's motor system caused by a loss of dopamine-producing brain cells. Approximately one and a half million Americans have the disease, and about 50,000 are diagnosed each year. The main symptoms are trembling in the hands, arms, legs, jaw, and face; stiffness of the limbs and trunk; slowed movement; and impaired balance and coordination. Symptoms of Parkinson's disease usually come on gradually and affect people over the age of 50, although there are rare forms that progress more quickly and strike at a younger age. There are currently no blood or laboratory tests for Parkinson's. Physicians must instead diagnose the disease based on the presence of symptoms and a patient's medical history.

This is a "Preliminary Research" report, which means the associations presented below still need to be confirmed by the scientific community. There is also an "Established Research" report on Parkinson's Disease that covers well-established associations for this condition.

**Gene or region: BST1**

SNP: rs4698412

This SNP is located on chromosome 4 (4p15.32) between the BST1 (or CD157) gene and the closely related CD38 gene. Both genes code for cell-surface proteins and research suggests that they may play a role in maintaining proper calcium levels. Although more research is needed to understand the potential role of these proteins in Parkinson's disease, it has been proposed that calcium levels are important for proper functioning of dopamine-producing brain cells, which are prematurely lost in individuals with Parkinson's disease. Multiple studies have identified an association between this SNP and Parkinson's disease in populations with European and Asian ancestry. In both populations, the A version of the SNP is associated with slightly increased risk for Parkinson's disease. The SNP has not been studied in populations with African ancestry.

**Citations**


**Gene or region: DGKQ**

SNP: rs11248060

This SNP is located on chromosome 4 (4p16.2) within the DGKQ gene, which encodes a protein called diacylglycerol kinase theta. More research is needed to define the potential role of this protein in Parkinson's disease. The SNP might also have been discovered because it serves as a signpost for a nearby, unidentified genetic factor that is related to Parkinson's disease. A large meta-analysis study consisting of about 16,000 people with Parkinson's disease and nearly 50,000 without the disease identified an association between this SNP and Parkinson's disease. In individuals with European ancestry, the T version of the SNP is associated with slightly increased risk for the disease. More research is needed to determine if this SNP is associated with Parkinson's in individuals with Asian or African ancestry.

**Citations**


**Gene or region: STK39**

SNP: rs2390669

This SNP is located on chromosome 2 (2q24.5) within the STK39 gene, which encodes a protein kinase that is thought to influence how cells respond to environmental stress. More research is needed to define the potential role of this protein in Parkinson's disease. The SNP might also have been discovered because it serves as a signpost for a nearby, unidentified genetic factor that is related to Parkinson's disease. A large meta-analysis study consisting of about 16,000 people with Parkinson's disease and nearly 50,000 without the disease identified an association between this SNP and Parkinson's disease. In individuals with European ancestry, the C version of the SNP is associated with slightly increased risk for the disease. More research is needed to determine if this SNP is associated with Parkinson's in individuals with Asian or African ancestry.

**Citations**


**Satake W et al. (2009). "Genome-wide association study identifies common variants at four loci as genetic risk factors for Parkinson's disease." Nat. Genet. 41(12):1303-7.**

Parkinson's Disease: Established Research

Established associations for this condition.
In this study, 23andMe researchers compared 3,426 individuals with Parkinson's disease to 29,624 individuals without the disease, all of European descent and participants in 23andMe research surveys. They found that individuals with the CC genotype at rs6812193 near the SCARB2 gene had about 1.2 times higher odds of Parkinson's disease compared to individuals with the CT genotype, and those with the TT genotype had about 1.2 times lower odds of Parkinson's disease.

**Genotype**  **What It Means**
CC  Slightly higher odds of developing Parkinson's disease.
CT  Typical odds of developing Parkinson's disease.
TT  Slightly lower odds of developing Parkinson's disease.

**Citations**