

## Documents

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**The Genetic Architecture of Parkinson's Disease in the AfrAbia Population: Current State and Future Perspectives**

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## Abstract

Over 80% of genetic studies in the Parkinson's disease (PD) field have been conducted on individuals of European descent. There is a social and scientific imperative to understand the genetic basis of PD across global populations for therapeutic development and deployment. PD etiology is impacted by genetic and environmental factors that are variable by ancestry and region, emphasising the need for worldwide programs to gather large numbers of patients to identify novel candidate genes and risk loci involved in disease. Only a handful of documented genetic assessments have investigated families with PD in AfrAbia, which comprises the member nations of the Arab League and the African Union, with very limited cohort and case-control studies reported. This review article summarises prior research on PD genetics in AfrAbia, highlighting gaps and challenges. We discuss the etiological risk spectrum in the context of historical interactions, highlighting allele frequencies, penetrance, and the clinical manifestations of known genetic variants in the AfrAbian PD patient community. © 2024 The Author(s).

## Author Keywords

AfrAbia; challenges; gaps; genetics; Parkinson's disease; prospects

## Index Keywords

gba1 protein, leucine rich repeat kinase 2, protein, unclassified drug; Africa, Arab, Berber, clinical feature, gene frequency, genetic profile, genetic risk, genetic variability, genetic variation, genetics, historical period, human, Parkinson disease, penetrance, Review, Saudi Arabia

## Chemicals/CAS

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## References

- Mazrui, AA.  
**The economic woman in Africa**  
(1992) *Finance & Development*, 29, pp. 42-43.
- Campbell, MC, Tishkoff, SA.  
**African genetic diversity: implications for human demographic history, modern human origins, and complex disease mapping**  
(2008) *Annual Review of Genomics and Human Genetics*, 9, pp. 403-433.
- (1993) *The Epidemiological Transition: Policy and Planning Implications for Developing Countries*, National Academies Press (US): Washington (DC)
- Verstraeten, A, Theuns, J, Van Broeckhoven, C.  
**Progress in unraveling the genetic etiology of Parkinson disease in a genomic era**  
(2015) *Trends in Genetics: TIG*, 31, pp. 140-149.

- Martin, I, Dawson, VL, Dawson, TM.  
**Recent advances in the genetics of Parkinson's disease**  
(2011) *Annual Review of Genomics and Human Genetics*, 12, pp. 301-325.
- Jasinska-Myga, B, Kachergus, J, Vilariño-Güell, C, Wider, C, Soto-Ortolaza, AI, Kefi, M  
**Comprehensive sequencing of the LRRK2 gene in patients with familial Parkinson's disease from North Africa**  
(2010) *Movement Disorders: Official Journal of the Movement Disorder Society*, 25, pp. 2052-2058.
- Zabetian, CP, Morino, H, Ujike, H, Yamamoto, M, Oda, M, Maruyama, H  
**Identification and haplotype analysis of LRRK2 G2019S in Japanese patients with Parkinson disease**  
(2006) *Neurology*, 67, pp. 697-699.
- Rizig, M, Bandres-Ciga, S, Makarious, MB, Ojo, OO, Crea, PW, Abiodun, OV  
**Identification of genetic risk loci and causal insights associated with Parkinson's disease in African and African admixed populations: a genome-wide association study**  
(2023) *The Lancet Neurology*, 22, pp. 1015-1025.
- Kim, SJ, Kiser, PK, Asfaha, S, DeKoter, RP, Dick, FA.  
**EZH2 inhibition stimulates repetitive element expression and viral mimicry in resting splenic B cells**  
(2023) *The EMBO Journal*, 42, p. e114462.
- Mohamed, W.  
**Leveraging genetic diversity to understand monogenic Parkinson's disease's landscape in AfrAbia**  
(2023) *American Journal of Neurodegenerative Disease*, 12, pp. 108-122.
- Mohamed, W.  
**Parkinson's genetics research on underrepresented AfrAbia populations: current state and future prospects**  
(2023) *American Journal of Neurodegenerative Disease*, 12, pp. 23-41.
- Bansal, VV, Kim, D, Reddy, B, Witmer, HDD, Dhiman, A, Godley, FA  
**Early Integrated Palliative Care Within a Surgical Oncology Clinic**  
(2023) *JAMA Network Open*, 6, p. e2341928.
- Wang, P, Cui, P, Luo, Q, Chen, J, Tang, H, Zhang, L  
**Penetrance of Parkinson disease LRRK2 G2385R-associated variant in the Chinese population**  
(2022) *European Journal of Neurology*, 29, pp. 2639-2644.
- Wang, P, Pan, J, Luo, Q, Chen, J, Tang, H, Chen, S  
**A 10-Year Community-Based Study of Leucine-Rich Repeat Kinase 2 G2385R Carriers' Conversion to Parkinson's Disease**  
(2022) *Movement Disorders: Official Journal of the Movement Disorder Society*, 37, pp. 1767-1772.

- Meeus, B, Nuytemans, K, Crosiers, D, Engelborghs, S, Peeters, K, Mattheijssens, M  
**Comprehensive genetic and mutation analysis of familial dementia with Lewy bodies linked to 2q35-q36**  
(2010) *Journal of Alzheimer's Disease: JAD*, 20, pp. 197-205.
- Corti, O, Lesage, S, Brice, A.  
**What genetics tells us about the causes and mechanisms of Parkinson's disease**  
(2011) *Physiological Reviews*, 91, pp. 1161-1218.
- Li, JQ, Tan, L, Yu, JT.  
**The role of the LRRK2 gene in Parkinsonism**  
(2014) *Molecular Neurodegeneration*, 9, p. 47.
- Schulte, C, Gasser, T.  
**Genetic basis of Parkinson's disease: inheritance, penetrance, and expression**  
(2011) *The Application of Clinical Genetics*, 4, pp. 67-80.
- Tomiyama, H, Li, Y, Funayama, M, Hasegawa, K, Yoshino, H, Kubo, SI  
**Clinicogenetic study of mutations in LRRK2 exon 41 in Parkinson's disease patients from 18 countries**  
(2006) *Movement Disorders: Official Journal of the Movement Disorder Society*, 21, pp. 1102-1108.
- Lesage, S, Patin, E, Condroyer, C, Leutenegger, AL, Lohmann, E, Giladi, N  
**Parkinson's disease-related LRRK2 G2019S mutation results from independent mutational events in humans**  
(2010) *Human Molecular Genetics*, 19, pp. 1998-2004.
- Benamer, HTS, de Silva, R.  
**LRRK2 G2019S in the North African population: a review**  
(2010) *European Neurology*, 63, pp. 321-325.
- Lesage, S, Leutenegger, AL, Ibanez, P, Janin, S, Lohmann, E, Dürr, A  
**LRRK2 haplotype analyses in European and North African families with Parkinson disease: a common founder for the G2019S mutation dating from the 13th century**  
(2005) *American Journal of Human Genetics*, 77, pp. 330-332.
- Warren, L, Gibson, R, Ishihara, L, Elango, R, Xue, Z, Akkari, A  
**A founding LRRK2 haplotype shared by Tunisian, US, European and Middle Eastern families with Parkinson's disease**  
(2008) *Parkinsonism & Related Disorders*, 14, pp. 77-80.
- Lucotte, G, David, D, Change, N.  
**New contribution on the LRRK2 G2019S mutation associated to Parkinson's disease: age estimation of a common**

**founder event of old age in Moroccan Berbers**

(2021) *International Journal of Modern Anthropology*, 1, pp. 11-22.

- Lucas-Sánchez, M, Serradell, JM, Comas, D.  
**Population history of North Africa based on modern and ancient genomes**  
(2021) *Human Molecular Genetics*, 30, pp. R17-R23.
- Dhimba, G, Muller, A, Lammertsma, K.  
**Chiral-at-Metal Racemization Unraveled for MX<sub>2</sub> (a-chel)<sub>2</sub> by Means of a Computational Analysis of MoO<sub>2</sub> (acnac)<sub>2</sub>**  
(2023) *Chemistry (Weinheim an Der Bergstrasse, Germany)*, 29, p. e202303605.
- Bandrés-Ciga, S, Mencacci, NE, Durán, R, Barrero, FJ, Escamilla-Sevilla, F, Morgan, S  
**Analysis of the genetic variability in Parkinson's disease from Southern Spain**  
(2016) *Neurobiology of Aging*, 37.  
210.e1–210.e5
- Richter, D, Grün, R, Joannes-Boyau, R, Steele, TE, Amani, F, Rué, M  
**The age of the hominin fossils from Jebel Irhoud, Morocco, and the origins of the Middle Stone Age**  
(2017) *Nature*, 546, pp. 293-296.
- Bouhouche, A, Tibar, H, Ben El Haj, R, El Bayad, K, Razine, R, Tazrout, S  
**LRRK2 G2019S Mutation: Prevalence and Clinical Features in Moroccans with Parkinson's Disease**  
(2017) *Parkinson's Disease*, 2017, p. 2412486.
- Watterson, GA, Guess, HA.  
**Is the most frequent allele the oldest?**  
(1977) *Theoretical Population Biology*, 11, pp. 141-160.
- Donnelly, P, Tavaré, S.  
**The ages of alleles and a coalescent**  
(1986) *Advances in Applied Probability*, 18, pp. 1-19.
- Diéterlen, F, Lucotte, G.  
**Original Synthetic Report: Origin of the G2019S mutation associated to Parkinson's disease in Europeans and in North Africans**  
(2010) *International Journal of Modern Anthropology*, 1, pp. 81-96.
- Bandrés-Ciga, S, Price, TR, Barrero, FJ, Escamilla-Sevilla, F, Pelegrina, J, Arepalli, S  
**Genome-wide assessment of Parkinson's disease in a Southern Spanish population**

(2016) *Neurobiology of Aging*, 45.  
213.e3–213.e9

- Campbell, CL, Palamara, PF, Dubrovsky, M, Botigué, LR, Fellous, M, Atzmon, G  
**North African Jewish and non-Jewish populations form distinctive, orthogonal clusters**  
(2012) *Proceedings of the National Academy of Sciences of the United States of America*, 109, pp. 13865-13870.
- Ben El Haj, R, Salmi, A, Regragui, W, Moussa, A, Bouslam, N, Tibar, H  
**Evidence for prehistoric origins of the G2019S mutation in the North African Berber population**  
(2017) *PloS One*, 12, p. e0181335.
- Change, N, Mercier, G, Lucotte, G.  
**Genetic screening of the G2019S mutation of the LRRK2 gene in Southwest European, North African, and Sephardic Jewish subjects**  
(2008) *Genetic Testing*, 12, pp. 333-339.
- Bokbot, Y, Pintado, JO, Rodriguez, AR, Santana, CGR, Amarir, A, Vasquez, J.V.  
(2005) *Le complexe funéraire et culturel d'Adrar Zerzem (Anti-Atlas, Maroc)*,  
(Accessed 5 June 2024)
- Schreier, J.  
**A Jewish riot against Muslims: The polemics of history in late colonial Algeria**  
(2016) *Comparative Studies in Society and History*, 58, pp. 746-773.
- Comtat, Emmanuelle  
(2009) *Les pieds-noirs et la politique*,  
(Accessed: 5 June 2024)
- Behar, DM, Saag, L, Karmin, M, Gover, MG, Wexler, JD, Sanchez, LF  
**The genetic variation in the R1a clade among the Ashkenazi Levites' Y chromosome**  
(2017) *Scientific Reports*, 7, p. 14969.
- Malamat, A.  
(1976) *A History of the Jewish People*,  
Harvard University Press: Tel Aviv
- Risch, N, de Leon, D, Ozelius, L, Kramer, P, Almasy, L, Singer, B  
**Genetic analysis of idiopathic torsion dystonia in Ashkenazi Jews and their recent descent from a small founder population**  
(1995) *Nature Genetics*, 9, pp. 152-159.

- Falk, R.  
**Genetic markers cannot determine Jewish descent**  
(2015) *Frontiers in Genetics*, 5, p. 462.
- Henn, BM, Botigué, LR, Gravel, S, Wang, W, Brisbin, A, Byrnes, JK  
**Genomic ancestry of North Africans supports back-to-Africa migrations**  
(2012) *PLoS Genetics*, 8, p. e1002397.
- Hulihan, MM, Ishihara-Paul, L, Kachergus, J, Warren, L, Amouri, R, Elango, R  
**LRRK2 Gly2019Ser penetrance in Arab-Berber patients from Tunisia: a case-control genetic study. The Lancet**  
(2008) *Neurology*, 7, pp. 591-594.
- Menozzi, E, Schapira, AHV.  
**Exploring the Genotype-Phenotype Correlation in GBA-Parkinson Disease: Clinical Aspects, Biomarkers, and Potential Modifiers**  
(2021) *Frontiers in Neurology*, 12, p. 694764.
- Skrahina, V, Gaber, H, Vollstedt, EJ, Förster, TM, Usnich, T, Curado, F  
**The Rostock International Parkinson's Disease (ROPAD) Study: Protocol and Initial Findings**  
(2021) *Movement Disorders: Official Journal of the Movement Disorder Society*, 36, pp. 1005-1010.
- Neumann, J, Bras, J, Deas, E, O'Sullivan, SS, Parkkinen, L, Lachmann, RH  
**Glucocerebrosidase mutations in clinical and pathologically proven Parkinson's disease**  
(2009) *Brain: a Journal of Neurology*, 132, pp. 1783-1794.
- Lim, JL, Lohmann, K, Tan, AH, Tay, YW, Ibrahim, KA, Abdul Aziz, Z  
**Glucocerebrosidase (GBA) gene variants in a multi-ethnic Asian cohort with Parkinson's disease: mutational spectrum and clinical features**  
(2022) *Journal of Neural Transmission (Vienna, Austria: 1996)*, 129, pp. 37-48.
- Stoker, TB, Camacho, M, Winder-Rhodes, S, Liu, G, Scherzer, CR, Foltynie, T  
**Impact of GBA1 variants on long-term clinical progression and mortality in incident Parkinson's disease**  
(2020) *Journal of Neurology, Neurosurgery, and Psychiatry*, 91, pp. 695-702.
- McNeill, A, Duran, R, Hughes, DA, Mehta, A, Schapira, AHV.  
**A clinical and family history study of Parkinson's disease in heterozygous glucocerebrosidase mutation carriers**  
(2012) *Journal of Neurology, Neurosurgery, and Psychiatry*, 83, pp. 853-854.
- Blauwendraat, C, Reed, X, Krohn, L, Heilbron, K, Bandres-Ciga, S, Tan, M  
**Genetic modifiers of risk and age at onset in GBA associated Parkinson's disease and Lewy body dementia**  
(2020) *Brain: a Journal of Neurology*, 143, pp. 234-248.

- Dinur, T, Becker-Cohen, M, Revel-Vilk, S, Zimran, A, Arkadir, D.  
**Parkinson's Clustering in Families of Non-Neuronopathic N370S GBA Mutation Carriers Indicates the Presence of Genetic Modifiers**  
(2021) *Journal of Parkinson's Disease*, 11, pp. 615-618.
- Choudhury, A, Aron, S, Botigué, LR, Sengupta, D, Botha, G, Bensellak, T  
**High-depth African genomes inform human migration and health**  
(2020) *Nature*, 586, pp. 741-748.
- Tolosa, E, Vila, M, Klein, C, Rascol, O.  
**LRRK2 in Parkinson disease: challenges of clinical trials**  
(2020) *Nature Reviews. Neurology*, 16, pp. 97-107.
- Lesage, S, Condroyer, C, Lannuzel, A, Lohmann, E, Troiano, A, Tison, F  
**Molecular analyses of the LRRK2 gene in European and North African autosomal dominant Parkinson's disease**  
(2009) *Journal of Medical Genetics*, 46, pp. 458-464.
- Day, JO, Mullin, S.  
**The Genetics of Parkinson's Disease and Implications for Clinical Practice**  
(2021) *Genes*, 12, p. 1006.
- MacArthur, DG, Manolio, TA, Dimmock, DP, Rehm, HL, Shendure, J, Abecasis, GR  
**Guidelines for investigating causality of sequence variants in human disease**  
(2014) *Nature*, 508, pp. 469-476.
- Farrer, MJ.  
**Doubts about TMEM230 as a gene for parkinsonism**  
(2019) *Nature Genetics*, 51, pp. 367-368.
- Tiffin, N.  
**Tiered informed consent: respecting autonomy, agency and individuality in Africa**  
(2018) *BMJ Global Health*, 3, p. e001249.
- Claw, KG, Anderson, MZ, Begay, RL, Tsosie, KS, Fox, K, Garrison, NA  
**A framework for enhancing ethical genomic research with Indigenous communities**  
(2018) *Nature Communications*, 9, p. 2957.
- Reardon, S.  
**Navajo Nation reconsiders ban on genetic research**  
(2017) *Nature*, 550, pp. 165-166.



- **Ten Years of the International Parkinson Disease Genomics Consortium: Progress and Next Steps**  
(2020) *Journal of Parkinson's Disease*, 10, pp. 19-30.
- **GP2: The Global Parkinson's Genetics Program**  
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