Supplementary Data: Frequency of the *LRRK2* G2019S mutation in South African patients with Parkinson's disease

Table S1 Demographics of the 647 South African PD probands

	N	**Mean AAO in years (SD)**	**Males N (%)**	**Mean AAO males (SD)**	**Mean AAO females (SD)**
All	647	57.5 (12.5)	375 (58%)	58.6 (12.5)	58.4 (12.6)
EOPD (< 50 years)	154 (24%)	40.3 (12.5)	94 (15%)	39.9 (12.5)	40.9 (12.5)
LOPD (≥ 50 years)	493 (76%)	62.8 (12.3)	281 (43%)	62.4 (12.5)	63.3 (12.2)
Ancestral origin	**European (Afrikaner)**	**European**	**African**	**Mixed ancestry**	**Asian Indian**
All	184 (28%)	195 (30%)	91 (14%)	171 (26%)	6 (1%)
EOPD (< 50 years)	54 (29%)	31(16%)	25 (27%)	41 (24%)	3 (50%)
LOPD (≥ 50 years)	130 (71%)	164 (84 %)	66 (73%)	130 (76%)	3 (50%)
Mean AAO (SD)	55.3 (12.5)	60.3 (12.4)	56.4 (12.6)	57.4 (12.5)	51.3 (12.1)
Mean AAO EOPD (SD)	39.9 (12.5)	41.3 (12.4)	41.9 (12.5)	40.4 (12.5)	37.3 (12.2)
Mean AAO LOPD (SD)	62.0 (12.2)	63.9 (12.2)	62.7 (12.5)	62.7 (12.3)	65.3 (11.5)
Family history	**Positive**	**Negative**	**Unknown**		
All	173 (27%)	466 (72%)	8 (1%)		
EOPD (< 50 years)	48 (28%)	105 (23%)	N/A		
LOPD (≥ 50 years)	125 (72%%)	361 (77%)	N/A		
Mean AAO (SD)	56.7 (12.5)	57.7 (12.6)	N/A		
Mean AAO EOPD (SD)	40.4 (12.5)	40.2 (12.5)	N/A		
Mean AAO LOPD (SD)	62.9 (12.4)	62.7 (12.5)	N/A		

AAO, Age at onset of PD; EOPD, Early-onset PD; LOPD, Late-onset PD; SD, Standard deviation; Mixed ancestry refers to a population unique to South Africa resulting from an admixture of individuals of African, European and Asian ancestral origins [Patterson *et al.* 2010].

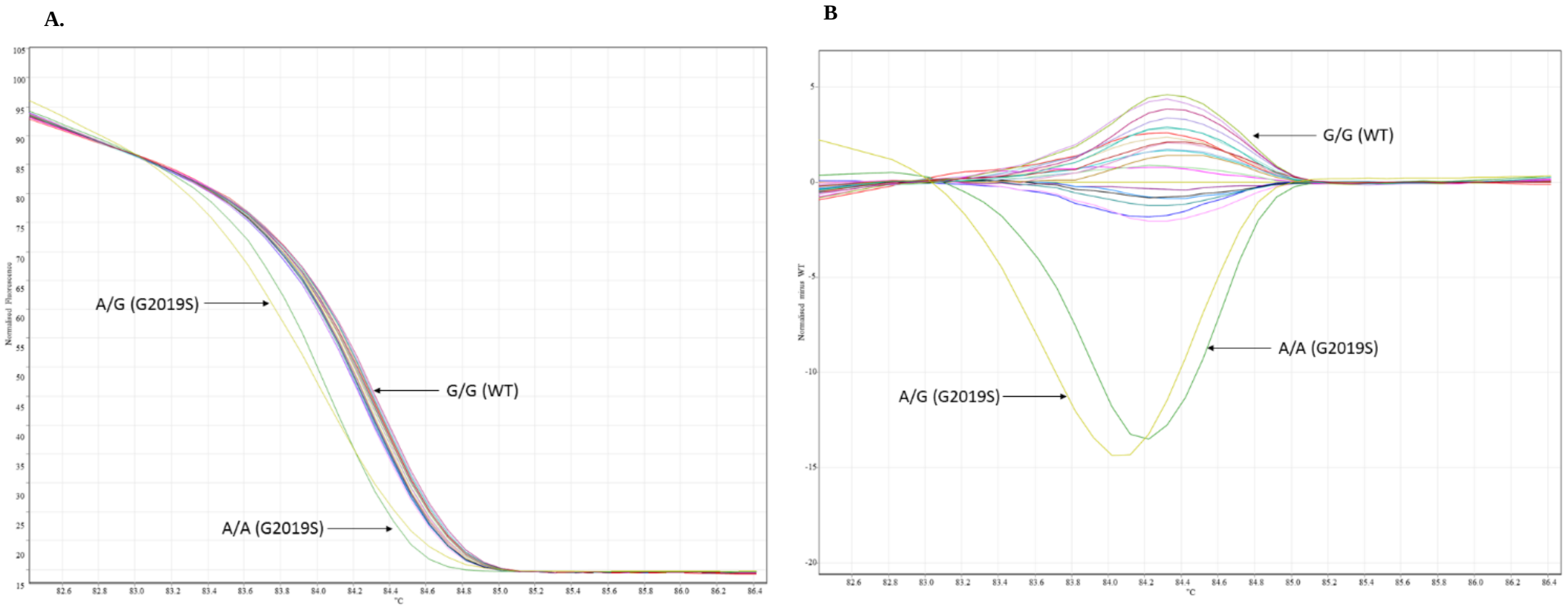
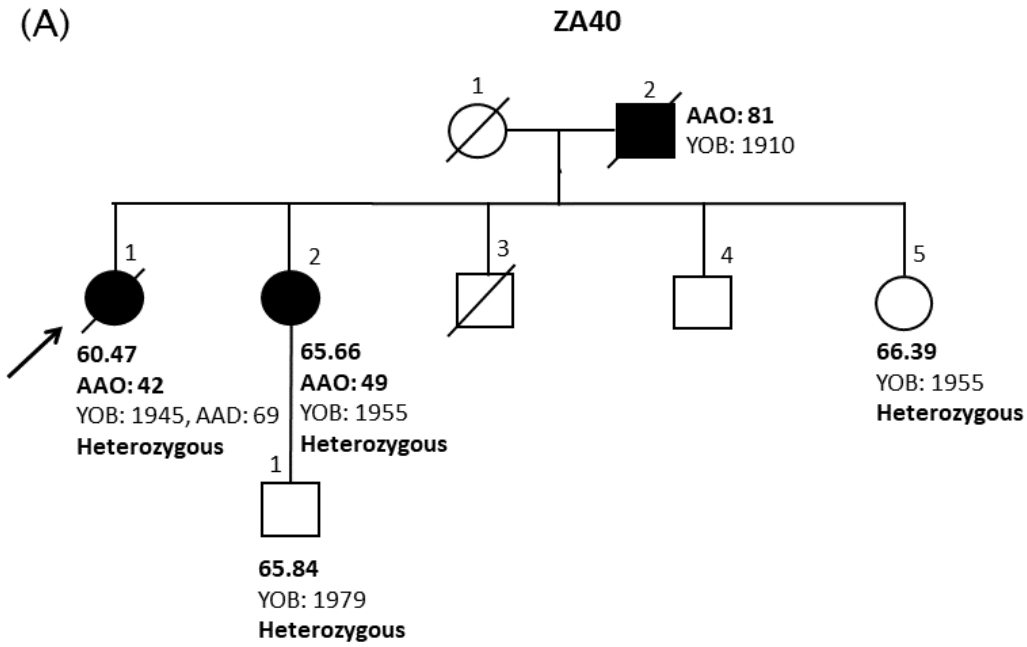


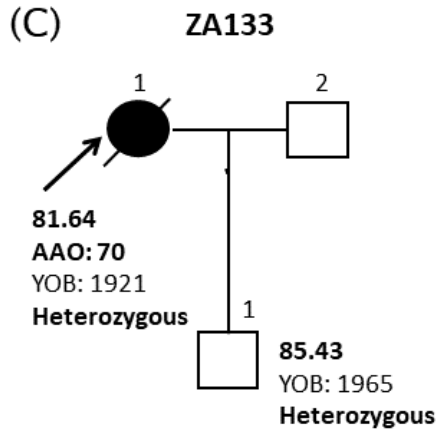
Figure S1 High-resolution melt (HRM) analysis of the *LRRK2* G2019S mutation. Normalization (A) and difference (B) graphs illustrate that heterozygous and homozygous forms of the mutation can clearly be distinguished from the wild-type.

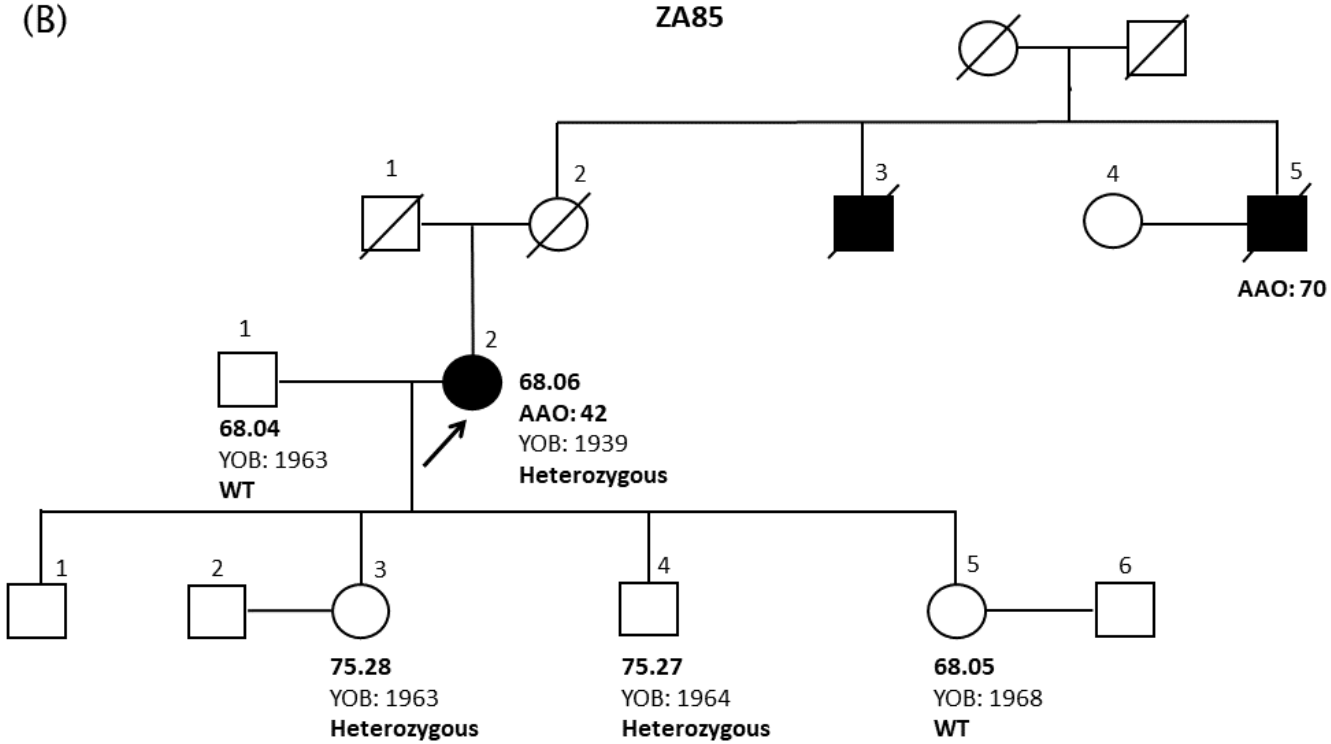
Table S2 Prevalence estimates with exact 95% binomial confidence intervals for detecting the G2019S mutation in South African Parkinson's disease patients.

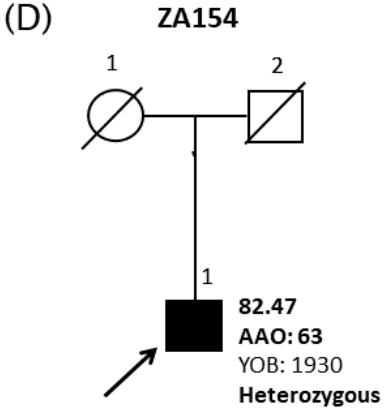
	N	Number of G2019S carriers	Prevalence (%)	Exact 95% CI (%)	
				Low	High
All	647	8	1.2	0.5	2.4
European (Afrikaner)	184	0	0	0	2.0
European	195	7	3.6	1.5	7.3
African	91	0	0	0	4.0
Mixed ancestry	171	1	0.6	0.02	3.2
Asian Indian	6	0	0	0	45.9

CI, confidence interval


(A)
ZA40
AAO: 81
YOB: 1910
60.47
AAO: 42
YOB: 1945, AAD: 69
Heterozygous
65.66
AAO: 49
YOB: 1955
Heterozygous
65.84
YOB: 1979
Heterozygous
66.39
YOB: 1955
Heterozygous


(C)
ZA133
81.64
AAO: 70
YOB: 1921
Heterozygous
85.43
YOB: 1965
Heterozygous


(B)
ZA85
AAO: 70
68.04
YOB: 1963
WT
68.06
AAO: 42
YOB: 1939
Heterozygous
75.28
YOB: 1963
Heterozygous
75.27
YOB: 1964
Heterozygous
68.05
YOB: 1968
WT


(D)
ZA154
82.47
AAO: 63
YOB: 1930
Heterozygous

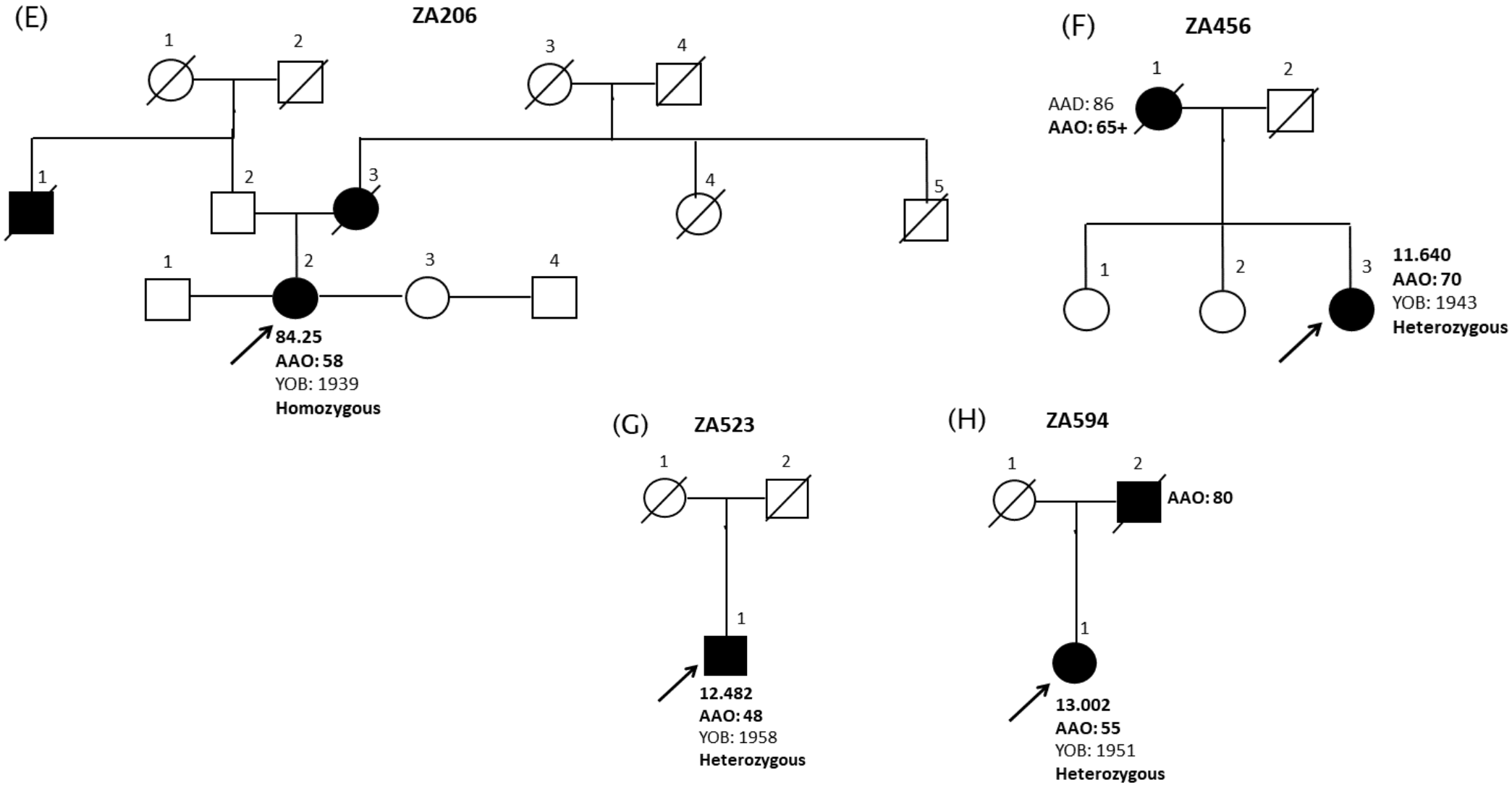


Figure S2 Pedigrees of families with *LRRK2* G2019S carriers.
The family number (ZA) is indicated above each pedigree. Males are indicated by a square and females are depicted as circles. The laboratory ID numbers, age at onset (AAO), date of birth (YOB), age at death (AAD; where known) and genotypes are indicated below each symbol. Filled in (black) symbols indicate affected individuals and deceased individuals are indicated with a diagonal strikethrough line. G2019S-positive individuals from families A, B, C and D were reported previously [Bardien *et al.*, 2010].

Table S3 Summary of published studies on *LRRK2* G2019S in sub-Saharan African populations

Reference	Country	Cohort	Sample size	Frequency of G2019S	Ancestry of G2019S carriers
Okubadejo et al., 2008	Nigeria	Unrelated patients	57 patients; 51 controls	None detected	-
Bardien et al., 2010	South Africa	Unrelated patients	205 patients	4/205 (2%)	Ashkenazi Jewish (3); Mixed ancestry (1)
Cilia et al., 2012	Ghana	Unrelated except for two siblings	54 patients; 46 controls	None detected	
Yonova-Doing et al., 2012	Zambia	Unrelated patients	39 patients; 181controls	None detected	-
Mahne et al., 2016	South Africa	Unrelated except for two siblings	16 patients	None detected	-
Okubadejo et al., 2018	Nigeria	Unrelated patients	126 patients; 54 controls	None detected	-
Present study	South Africa	Unrelated patients	647 patients	8/647 (1.2%)	Ashkenazi Jewish (7); Mixed ancestry (1)

References

1. Patterson N, Petersen DC, van der Ross RE, et al (2010) Genetic structure of a unique admixed population: implications for medical research. Hum Mol Genet 19:411–419. https://doi.org/10.1093/hmg/ddp505

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3. Okubadejo N, Britton A, Crews C, et al (2008) Analysis of Nigerians with apparently sporadic Parkinson disease for mutations in LRRK2, PRKN and ATXN3. PLoS One 3:e3421. https://doi.org/10.1371/journal.pone.0003421

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7. Okubadejo NU, Rizig M, Ojo OO, et al (2018) Leucine Rich Repeat Kinase 2 (LRRK2) Gly2019Ser Mutation Is Absent In A Second Cohort Of Nigerian Africans With Parkinson Disease. PLoS One 363945. https://doi.org/10.1101/363945