Supplementary Table 1: Descriptive Statistics of Individual Sites

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Site | Country | No. of PD Cases | No. of Controls | No. (%) of Males in PD cases | No. (%) of Males in Controls | Mean(SD) Age in PD Cases | Mean(SD) Age in controls | Diagnostic Criteria |
| Caucasian series |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
| Aasly | Norway | 527 | 510 | 314 (59%) | 276 (54%) | 73.8 (10.6) | 71.1 (10.6) | UKPDBB |
| Annesi | Italy | 178 | 182 | 98 (53.6%) | 93 (51.1%) | 65.6 (9) | 61.9 (9) | UKPDBB |
| Bozi | Greece | 113 | 104 | 55 (48.7%) | 49 (47.1%) | 75.7 (7.3) | 73.0 (7.3) | UKPDBB |
| Brice | France | 272 | 231 | 168 (61.8%) | 132 (57.1%) | 57.7 (11.5) | 57.8 (11.5) | UKPDBB |
| Garraux | Belgium | 64 | 14 | 34 (53.1%) | 7 (50%) | 70.5 (9.6) | 66.1 (9.6) | UKPDBB |
| Hadjigeorgiou | Greece | 313 | 328 | 170 (54.3%) | 169 (51.5%) | 64.7 (9.8) | 63.2 (9.8) | UKPDBB |
| Lynch/Ross | Ireland | 328 | 345 | 183 (55.8%) | 121 (35.1%) | 68.1 (10.3) | 73.4 (10.3) | UKPDBB |
| Maragonore | USA | 801 | 223 | 491 (62.4%) | 109 (62.6%) | 61.7 (11) | NA | UKPDBB |
| Mellick | Australia | 893 | 916 | 556 (62.3%) | 373 (40.7%) | 73.6 (11.1) | 71.7 (11.1) | Bower |
| Morrison | England | 723 | 349 | 490 (67.8%) | 87 (25.1%) | 66.2 (10.8) | NA | UKPDBB |
| Opala/Ross | Poland | 291 | 255 | 186 (63.9%) | 113 (44.3%) | 70.9 (10.5) | 65.0 (10.5) | UKPDBB |
| van Broeckhoven | Belgium | 497 | 510 | 286 (57.1%) | 214 (42.1%) | 68.1 (10.6) | 64.7 (10.6) | Pals/ Gelb |
| Wirdefeldt | Sweden | 77 | 194 | 41 (53.2%) | 93 (47.9%) | 72.3 (8.4) | 71.0 (8.4) | UKPDBB |
| Wszolek/Ross | USA | 692 | 827 | 440 (63.6%) | 354 (42.8%) | 74.6 (11.4) | 70.1 (11.4) | UKPDBB |
| Total |  | 7715 | 8261 |  |  |  |  |  |
| Asian series |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
| Chung | Korea | 368 | 333 | 153 (41.6%) | 140 (42%) | 58 (9.6) | 66.1 (9.6) | UKPDBB |
| Lin | Taiwan | 160 | 160 | 80 (50%) | 80 (50%) | 70.8 (9.8) | 70.8 (9.8) | UKPDBB |
| Mok | China | 259 | 78 | 158 (61.5%) | 52 (66.7%) | 64.8 (4.1) | 62.5 (4.1) | UKPDBB |
| Satake/Toda | Japan | 988 | 2521 | 405 (41.0%) | 1525 (60.5%) | 58.8 (10.1) | 49.9 (14.2) | UKPDBB |
| Tan | Singapore | 171 | 181 | 110 (64.3%) | 112 (61.9%) | 62.4 (9.3) | 45.2 (9.3) | UKPDBB |
| Total |  | 1946 | 3273 |  |  |  |  |  |

No.= number, NA indicates that data was unavailable

Supplementary Table 2: Associations and Minor Allele Frequency (MAF) of individual *LRRK2* and *PARK16* variants with risk of PD in Caucasian and Asian Series. MAF was calculated separately for Asian and Caucasian series.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Caucasian Series |  |  |  |  |
| SNP | MAF | Minor Allele | OR | Pvalue |
| *LRRK2* rs1491946 | 21.2% | C | 1.16 (1.10 ,1.24) | <0.001 |
| *LRRK2* rs7133914 | 6.9% | A | 0.93 (0.81 ,1.08) | 0.36 |
| *PARK16* rs708273 | 42.6% | T | 1.03 (0.97 ,1.09) | 0.32 |
| *PARK16* rs708725 | 48.4% | C | 0.91 (0.86 ,0.97) | 0.004 |
| *PARK16* rs823139 | 12.0% | T | 0.91 (0.84 ,1.00) | 0.038 |
| *PARK16* rs823156 | 18.2% | G | 0.94 (0.87 ,1.01) | 0.09 |
| *PARK16* rs11240572 | 3.3% | A | 1.09 (0.93 ,1.28) | 0.28 |
| Asian Series |  |  |  |  |
| SNP | MAF | Minor Allele | OR | Pvalue |
| *LRRK2* rs1491946 | 31.8% | C | 1.10 (1.00 ,1.21) | 0.03 |
| *PARK16* rs708723 | 14.0% | T | 1.76 (1.30 ,2.35) | <0.001 |
| *PARK16* rs708725 | 47.3% | C | 0.82 (0.75 ,0.90) | <0.001 |
| *PARK16* rs823139 | 14.1% | T | 0.78 (0.69 ,0.88) | <0.001 |
| *PARK16* rs823156 | 20.7% | G | 0.76 (0.68 ,0.85) | <0.001 |
| *PARK16* rs11240572 | 14.7% | A | 0.78 (0.68 ,0.89) | <0.001 |

OR (Odds Ratio)

Supplementary Table 3: Evaluation of interactions of *LRRK2* rs1491942 and *PARK16* variants with regard to susceptibility to Parkinson’s disease in the Combined Series

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| *LRRK2* Variant/Genotype | *PARK16* Variant/Genotype | Sample genotype count and frequency | Test of Association OR | p-value | Models for the *LRRK2* and *PARK16* SNPs and Test of Interaction Results |
|  |  |  |  |  |  |
| *LRRK2* rs1491942 | rs708273 |  |  |  | Additive/Additive Model |
| GG | GG | 2601 (21.7%) | 1.00 (reference) | N/A | OR: 1.0 (0.9, 1.11) |
| GG | GT | 3288 (27.5%) | 1.02 (0.92, 1.10) | 0.75 | p=0.98 |
| GG | TT | 1185 (9.9%) | 1.02 (0.9, 1.15) | 0.75 |  |
| GC | GG | 1725 (14.4%) | 1.11 (0.94, 1.30) | 0.21 | Heterogeneity: I2=0, p=0.49 |
| GC | GT | 1824 (15.2%) | 1.08 (0.94, 1.24) | 0.25 |  |
| GC | TT | 673 (5.6%) | 1.2 (1.04, 1.37) | 0.011 |  |
| CC | GG | 315 (2.6%) | 1.11 (0.9, 1.35) | 0.32 |  |
| CC | GT | 260 (2.2%) | 1.37 (1.06, 1.78) | 0.018 |  |
| CC | TT | 93 (0.8%) | 1.64 (1.21, 2.22) | 0.001 |  |
| *LRRK2* rs1491942 | rs708725 |  |  |  | Additive/Additive Model |
| GG | TT | 2291 (15.8%) | 1.00 (reference)) | N/A | OR: 0.98 (0.90, 1.06) |
| GG | TC | 3884 (26.7%) | 0.85 (0.76, 0.95) | 0.00365 | p=0.55 |
| GG | CC | 2066 (14.2%) | 0.82 (0.72, 0.94) | 0.00332 |  |
| GC | TT | 1579 (10.9%) | 1.22 (1.06, 1.39) | 0.00418 | Heterogeneity: I2=0, p=0.12 |
| GC | TC | 2510 (17.3%) | 0.9 (0.8, 1.02) | 0.0968 |  |
| GC | CC | 1266 (8.7%) | 0.91 (0.78, 1.06) | 0.237 |  |
| CC | TT | 249 (1.7%) | 1.38 (1.05, 1.82) | 0.0227 |  |
| CC | TC | 448 (3.1%) | 1.14 (0.92, 1.41) | 0.232 |  |
| CC | CC | 228 (1.6%) | 1.15 (0.85, 1.54) | 0.372 |  |
| *LRRK2* rs1491942 | rs823139 |  |  |  | Additive/Additive Model |
| GG | GG | 6825 (43.6%) | 1.00 (reference) | N/A | OR: 1.01 (0.92, 1.11) |
| GG | GT | 1945 (12.4%) | 0.82 (0.74, 0.92) | 0.00036 | p=0.87 |
| GG | TT | 144 (0.9%) | 1.08 (0.76, 1.53) | 0.663 |  |
| GC | GG | 4331 (27.7%) | 1.12 (1.04, 1.22) | 0.00483 | Heterogeneity: I2=0, p=0.56 |
| GC | GT | 1295 (8.3%) | 0.91 (0.8, 1.03) | 0.154 |  |
| GC | TT | 103 (0.7%) | 1.08 (0.72, 1.62) | 0.702 |  |
| CC | GG | 762 (4.9%) | 1.35 (1.15, 1.58) | 0.000244 |  |
| CC | GT | 218 (1.4%) | 1.25 (0.94, 1.66) | 0.127 |  |
| CC | TT | 16 (0.1%) | 0.7 (0.25, 1.96) | 0.491 |  |
| *LRRK2* rs1491942 | rs823156 |  |  |  | Additive/AdditiveModel |
| GG | AA | 5734 (37.6%) | 1.00 (reference) | N/A | OR: 0.99 (0.88, 1.11) |
| GG | AG | 2580 (16.9%) | 0.89 (0.81, 0.98) | 0.0228 | p=0.83 |
| GG | GG | 346 (2.3%) | 0.76 (0.6, 0.96) | 0.0204 |  |
| GC | AA | 3687 (24.2%) | 1.14 (1.05, 1.24) | 0.00316 | Heterogeneity: I2=33, p=0.56 |
| GC | AG | 1681 (11%) | 0.98 (0.87, 1.1) | 0.679 |  |
| GC | GG | 234 (1.5%) | 0.95 (0.72, 1.27) | 0.744 |  |
| CC | AA | 635 (4.2%) | 1.32 (1.11, 1.57) | 0.00148 |  |
| CC | AG | 285 (1.9%) | 1.29 (1.01, 1.67) | 0.0453 |  |
| CC | GG | 55 (0.4%) | 0.97 (0.54, 1.75) | 0.92 |  |
| *LRRK2* rs1491942 | rs11240572 |  |  |  | Additive/Dominant Model |
| GG | CC | 7839 (50%) | 1.00 (reference) | N/A | OR: 0.87 (0.74, 1.01) |
| GG | CA+AA | 1095 (7%) | 0.99 (0.86, 1.13) | 0.844 | p=0.069 |
| GC | CC | 4903 (31.3%) | 1.14 (1.06, 1.23) | 0.000512 |  |
| GC | CA+AA | 834 (5.3%) | 0.91 (0.78, 1.06) | 0.234 | Heterogeneity: I2=0, p=0.99 |
| CC | CC | 834 (5.3%) | 1.39 (1.19, 1.62) | 2.16E-05 |  |
| CC | CA+AA | 167 (1.1%) | 1.13 (0.82, 1.57) | 0.447 |  |

OR (Odds Ratio), Tests of Interaction presents results of Fixed Effects Model with OR and 95% Confidence Interval (CI), Models were either *LRRK2* Additive/*PARK16* Additive, *LRRK2* Additive/*PARK16* Dominant, or *LRRK2* Dominant/*PARK16* Dominant (when MAF<15%, then Dominant scheme was used)

Supplementary Table 4: Evaluation of interactions of *LRRK2* rs1491942 and *PARK16* variants with regard to susceptibility to Parkinson’s disease in the Caucasian Series

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| *LRRK2* Variant/Genotype | *PARK16* Variant/Genotype | Sample genotype count and frequency | Test of Association OR | p-value | Models for the *LRRK2* and *PARK16* SNPs and Test of Interaction Results |
|  |  |  | OR | p-value |  |
| *LRRK2* rs1491942 | rs708273 |  |  |  | Additive/AdditiveModel |
| GG | GG | 2091 (20.2%) | 1.00 (reference) | N/A | OR: 1.0 (0.88, 1.14) |
| GG | GT | 3203 (30.9%) | 1.02 (0.91, 1.14) | 0.72 | p=0.95 |
| GG | TT | 1130 (10.9%) | 1.14 (0.99, 1.33) | 0.074 |  |
| GC | GG | 1111 (10.7%) | 1.12 (0.96, 1.3) | 0.15 | Heterogeneity: I2=0, p=0.48 |
| GC | GT | 1730 (16.7%) | 1.19 (1.04, 1.36) | 0.009 |  |
| GC | TT | 625 (6%) | 1.08 (0.9, 1.30) | 0.39 |  |
| CC | GG | 155 (1.5%) | 1.61 (1.15, 2.27) | 0.006 |  |
| CC | GT | 230 (2.2%) | 1.55 (1.17, 2.06) | 0.002 |  |
| CC | TT | 74 (0.7%) | 1.52 (0.93, 2.48) | 0.092 |  |
| *LRRK2* rs1491942 | rs708725 |  |  |  | Additive/Additive Model |
| GG | TT | 1626 (17.1%) | 1.00 (reference) | N/A | OR: :1.02 (0.88, 1.18) |
| GG | TC | 2728 (28.7%) | 0.89 (0.78, 1.01) | 0.066 | p=0.83 |
| GG | CC | 1540 (16.2%) | 0.85 (0.73, 0.99) | 0.042 |  |
| GC | TT | 960 (10.1%) | 1.17 (1.00, 1.38) | 0.058 | Heterogeneity: I2=0, p=0.16 |
| GC | TC | 1481 (15.6%) | 0.95 (0.82, 1.10) | 0.51 |  |
| GC | CC | 770 (8.1%) | 0.96 (0.79, 1.16) | 0.66 |  |
| CC | TT | 116 (1.2%) | 1.33 (0.9, 1.96) | 0.16 |  |
| CC | TC | 194 (2%) | 1.52 (1.11, 2.08) | 0.009 |  |
| CC | CC | 100 (1.1%) | 1.26 (0.8, 1.98) | 0.33 |  |
| *LRRK2* rs1491942 | rs823139 |  |  |  | Additive/Additive Model |
| GG | GG | 5035 (48.1%) | 1.00 (reference) | N/A | OR: 0.99 (0.90, 1.10) |
| GG | GT | 1374 (13.1%) | 0.86 (0.76, 0.98) | 0.018 | p=0.59 |
| GG | TT | 91 (0.9%) | 1.11 (0.72, 1.71) | 0.63 |  |
| GC | GG | 2708 (25.9%) | 1.11 (1.01, 1.22) | 0.03 | Heterogeneity: I2=0, p=0.54 |
| GC | GT | 742 (7.1%) | 0.97 (0.83, 1.14) | 0.71 |  |
| GC | TT | 58 (0.6%) | 1.19 (0.70, 2.02) | 0.52 |  |
| CC | GG | 361 (3.4%) | 1.46 (1.17, 1.83) | <0.001 |  |
| CC | GT | 91 (0.9%) | 1.69 (1.08, 2.64) | 0.021 |  |
| CC | TT | 10 (0.1%) | 0.65 (0.18, 2.32) | 0.50 |  |
| *LRRK2* rs1491942 | rs823156 |  |  |  | Additive/Additive Model |
| GG | AA | 4151 (41.2%) | 1.00 (reference) | N/A | OR: 0.95 (0.86, 1.05) |
| GG | AG | 1882 (18.7%) | 0.94 (0.84, 1.05) | 0.27 | p=0.87 |
| GG | GG | 209 (2.1%) | 0.87 (0.66, 1.16) | 0.35 |  |
| GC | AA | 2278 (22.6%) | 1.12 (1.01, 1.25) | 0.034 | Heterogeneity: I2=23, p=0.37 |
| GC | AG | 996 (9.9%) | 1.12 (0.97, 1.30) | 0.11 |  |
| GC | GG | 108 (1.1%) | 0.84 (0.56, 1.24) | 0.38 |  |
| CC | AA | 301 (3%) | 1.48 (1.15, 1.89) | 0.002 |  |
| CC | AG | 124 (1.2%) | 1.59 (1.09, 2.32) | 0.016 |  |
| CC | GG | 17 (0.2%) | 0.84 (0.31, 2.22) | 0.72 |  |
| *LRRK2* rs1491942 | rs11240572 |  |  |  | Additive/Dominant Model |
| GG | CC | 6094 (57.9%) | 1.00 (reference) | N/A | OR:0.89 (0.68, 1.17) |
| GG | CA+AA | 434 (4.1%) | 1.15 (0.94, 1.40) | 0.17 | p=0.25 |
| GC | CC | 3300 (31.4%) | 1.12 (1.03, 1.23) | 0.009 |  |
| GC | CA+AA | 223 (2.1%) | 1.06 (0.81, 1.40) | 0.67 | Heterogeneity: I2=0, p=0.87 |
| CC | CC | 433 (4.1%) | 1.51 (1.23, 1.86) | <0.001 |  |
| CC | CA+AA | 33 (0.3%) | 1.65 (0.8, 3.40) | 0.17 |  |

OR (Odds Ratio), Tests of Interaction presents results of Fixed Effects Model with OR and 95% Confidence Interval (CI), Models were either *LRRK2* Additive/*PARK16* Additive, *LRRK2* Additive/*PARK16* Dominant, or *LRRK2* Dominant/*PARK16* Dominant (when MAF<15%, then Dominant scheme was used)

Supplementary Table 5: Evaluation of interactions of *LRRK2* rs1491942 and *PARK16* variants with regard to susceptibility to Parkinson’s disease in the Asian Series

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| *LRRK2* Variant/Genotype | *PARK16* Variant/Genotype | Sample genotype count and frequency | Test of Association OR | p-value | Models for the *LRRK2* and *PARK16* SNPs and Test of Interaction Results |
| *LRRK2* rs1491942 | rs708723 |  |  |  | Additive/Additive Model |
| GG | GG | 510 (31.6%) | 1.00 (reference) | N/A | OR: 1.1 (0.89, 1.36) |
| GG | GT | 85 (5.3%) | 2.72 (1.53, 4.83) | <0.001 | p=0.40 |
| GG | TT | 55 (3.4%) | 1.96 (0.97, 3.95) | 0.060 |  |
| GC | GG | 614 (38%) | 1.01 (0.8, 1.28) | 0.91 | Heterogeneity: I2=0, p=0.43 |
| GC | GT | 94 (5.8%) | 4.11 (2.21, 7.65) | <0.001 |  |
| GC | TT | 48 (3%) | 2.94 (1.31, 6.56) | 0.009 |  |
| CC | GG | 160 (9.9%) | 1.15 (0.81, 1.65) | 0.43 |  |
| CC | GT | 30 (1.9%) | 2.69 (1.07, 6.8) | 0.036 |  |
| CC | TT | 19 (1.2%) | 4.41 (1.22, 15.9) | 0.024 |  |
| *LRRK2* rs1491942 | rs708725 |  |  |  | Additive/Additive Model |
| GG | TT | 665 (13.3%) | 1.00 (reference) | N/A | OR: 0. 97 (0.86, 1.11) |
| GG | TC | 1156 (23.1%) | 0.76 (0.62, 0.94) | 0.01 | p=0.69 |
| GG | CC | 526 (10.5%) | 0.74 (0.58, 0.96) | 0.0237 |  |
| GC | TT | 619 (12.4%) | 1.25 (0.99, 1.58) | 0.0614 | Heterogeneity: I2=0, p=0.19 |
| GC | TC | 1029 (20.6%) | 0.8 (0.65, 0.99) | 0.0411 |  |
| GC | CC | 496 (9.9%) | 0.82 (0.63, 1.06) | 0.124 |  |
| CC | TT | 133 (2.7%) | 1.35 (0.9, 2) | 0.142 |  |
| CC | TC | 254 (5.1%) | 0.85 (0.62, 1.16) | 0.302 |  |
| CC | CC | 128 (2.6%) | 1 (0.67, 1.51) | 0.982 |  |
| *LRRK2* rs1491942 | rs823139 |  |  |  | Additive/Additive Model |
| GG | GG | 1790 (34.6%) | 1.00 (reference) | N/A | OR: 1.08 (0.93, 1.26) |
| GG | GT | 571 (11%) | 0.72 (0.58, 0.89) | 0.00223 | p=0.31 |
| GG | TT | 53 (1%) | 1 (0.55, 1.81) | 0.993 |  |
| GC | GG | 1623 (31.4%) | 1.12 (0.97, 1.29) | 0.133 | Heterogeneity: I2=0, p=0.23 |
| GC | GT | 553 (10.7%) | 0.81 (0.66, 1) | 0.0508 |  |
| GC | TT | 45 (0.9%) | 0.92 (0.48, 1.74) | 0.791 |  |
| CC | GG | 401 (7.8%) | 1.21 (0.96, 1.52) | 0.112 |  |
| CC | GT | 127 (2.5%) | 0.96 (0.65, 1.42) | 0.839 |  |
| CC | TT | 6 (0.1%) | 0.79 (0.14, 4.51) | 0.791 |  |
| *LRRK2* rs1491942 | rs823156 |  |  |  | Additive/Additive Model |
| GG | AA | 1583 (30.6%) | 1.00 (reference) | N/A | OR: 0.99 (0.82, 1.12) |
| GG | AG | 698 (13.5%) | 0.76 (0.62, 0.93) | 0.00658 | p=0.92 |
| GG | GG | 137 (2.6%) | 0.53 (0.35, 0.82) | 0.00388 |  |
| GC | AA | 1409 (27.2%) | 1.14 (0.97, 1.33) | 0.103 | Heterogeneity: I2=16 p=0.29 |
| GC | AG | 685 (13.2%) | 0.74 (0.61, 0.91) | 0.00352 |  |
| GC | GG | 126 (2.4%) | 0.98 (0.64, 1.52) | 0.94 |  |
| CC | AA | 334 (6.5%) | 1.13 (0.88, 1.46) | 0.326 |  |
| CC | AG | 161 (3.1%) | 1.02 (0.72, 1.46) | 0.893 |  |
| CC | GG | 38 (0.7%) | 0.92 (0.43, 1.99) | 0.835 |  |
| *LRRK2* rs1491942 | rs11240572 |  |  |  | Additive/Dominant Model |
| GG | CC | 1745 (33.9%) | 1.00 (reference) | N/A | OR:0.92 (0.75, 1.13) |
| GG | CA+AA | 661 (12.8%) | 0.85 (0.7, 1.04) | 0.116 | p=0.42 |
| GC | CC | 1603 (31.1%) | 1.17 (1.01, 1.35) | 0.039 |  |
| GC | CA+AA | 611 (11.9%) | 0.82 (0.67, 1.01) | 0.0633 | Heterogeneity: I2=0, p=0.87 |
| CC | CC | 401 (7.8%) | 1.23 (0.97, 1.55) | 0.0825 |  |
| CC | CA+AA | 134 (2.6%) | 1 (0.68, 1.45) | 0.981 |  |

OR (Odds Ratio), Tests of Interaction presents results of Fixed Effects Model with OR and 95% Confidence Interval (CI), Models were either *LRRK2* Additive/*PARK16* Additive, *LRRK2* Additive/*PARK16* Dominant, or *LRRK2* Dominant/*PARK16* Dominant (when MAF<15%, then Dominant scheme was used)

Supplementary Table 6: Stratified Analysis of Effect of *LRRK2* rs1491942 on Carriers and Non-carriers of *PARK16* rs11240572 Minor Allele

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | *PARK16* rs11240572 allele | | |  |  |
|  | Carriers |  |  | Non-Carriers |  |  |
| Ethnic Series | *LRRK2* OR (95% CI) | pval | n | *LRRK2* OR (95% CI) | pval | n |
| Asian | 1.02 (0.85 ,1.22) | 0.82 | 1409 | 1.13 (1.58 ,1.10) | 0.17 | 3766 |
| Caucasian | 1.04 (0.80 ,1.35) | 0.79 | 697 | 1.17 (1.10 ,1.25) | <0.000 | 9995 |
| Combined | 1.03 (0.88 ,1.19) | 0.73 | 2106 | 1.15 (0.10 ,1.22) | <0.000 | 13761 |

Supplementary Table 7: Evaluation of interactions of *LRRK2* rs7133914 and *PARK16* variants with regard to susceptibility to Parkinson’s disease in the Caucasian Series

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| *LRRK2* Variant/Genotype | *PARK16* Variant/Genotype | sample genotype count and frequency | Test of Association OR | p-value | Models for the *LRRK2* and *PARK16* SNPs and Test of Interaction Results |
|  |  |  |  |  |  |
| *LRRK2* rs7133914 | rs708273 |  |  |  | Dominant/Additive Model |
| GG | GG | 1788 (27.9%) | 1.00 (reference) | N/A | OR: 0.92 (0.69, 1.20) |
| GG | GT | 3764 (58.7%) | 1.02 (0.91, 1.16) | 0.71 | p=0.54 |
| GG | TT | 288 (4.5%) | 1.10 (0.94, 1.30) | 0.22 |  |
| GA+AA | GG | 577 (9%) | 1.07 (0.83, 1.39) | 0.60 | Heterogeneity: I2=35 p=0.11 |
| GA+AA | GT | 1361 (22.7%) | 0.88 (0.71, 1.10) | 0.26 |  |
| GA+AA | TT | 3834 (63.9%) | 0.96 (0.69, 1.33) | 0.79 |  |
| *LRRK2* rs7133914 | rs708725 |  |  |  | Dominant/Additive Model |
| GG | TT | 206 (3.4%) | 1.00 (reference) | N/A | Additive Model |
| GG | TC | 600 (10%) | 0.92 (0.8, 1.06) | 0.24 | OR: 0.85(0.61, 1.18) |
| GG | CC | 4317 (66.4%) | 0.79 (0.66, 0.94) | 0.008 | p=0.33 |
| GA+AA | TT | 1306 (20.1%) | 0.89 (0.66, 1.20) | 0.44 |  |
| GA+AA | TC | 688 (10.6%) | 0.72 (0.57, 0.91) | 0.006 | Heterogeneity: I2=0, p=0.61 |
| GA+AA | CC | 188 (2.9%) | 1.02 (0.74, 1.40) | 0.91 |  |
| *LRRK2* rs7133914 | rs823139 |  |  |  | Dominant/Additive Model |
| GG | GG | 3658 (58.1%) | 1.00 (reference) | N/A | Additive Model |
| GG | GT | 1799 (28.6%) | 0.92 (0.81, 1.05) | 0.22 | OR: 1.20(0.97, 1.48) |
| GG | TT | 573 (9.1%) | 1.00 (0.65, 1.53) | 0.99 | p=0.096 |
| GA+AA | GG | 270 (4.3%) | 0.98 (0.83, 1.15) | 0.80 |  |
| GA+AA | GT | 5486 (84%) | 0.72 (0.53, 0.98) | 0.034 | Heterogeneity: I2=13, p=0.25 |
| GA+AA | TT | 169 (2.6%) | 1.26 (0.34, 4.64) | 0.73 |  |
| *LRRK2* rs7133914 | rs823156 |  |  |  | Dominant/Additive Model |
| GG | AA | 848 (13%) | 1.00 (reference) | N/A | Additive Model |
| GG | AG | 26 (0.4%) | 1.00 (0.89, 1.13) | 0.96 | OR: 0.88 (0.72, 1.09) |
| GG | GG | 5281 (80.9%) | 0.83 (0.60, 1.13) | 0.24 | p=0.25 |
| GA+AA | AA | 370 (5.7%) | 0.97 (0.81, 1.17) | 0.77 |  |
| GA+AA | AG | 805 (12.3%) | 0.79 (0.60, 1.03) | 0.078 | Heterogeneity:I2=0. p=0.74 |
| GA+AA | GG | 70 (1.1%) | 1.13 (0.49, 2.64) | 0.77 |  |
| *LRRK2* rs7133914 | rs11240572 |  |  |  | Dominant/Dominant Model |
| GG | CC | 1730 (16.7%) | 1.00 (reference) | N/A | OR: 1.20 (0.70, 2.07) |
| GG | CA+AA | 625 (6%) | 1.05 (0.84, 1.30) | 0.69 | p=0.51 |
| GA+AA | CC | 155 (1.5%) | 0.91 (0.78, 1.06) | 0.25 |  |
| GA+AA | CA+AA | 230 (2.2%) | 1.15 (0.71, 1.86) | 0.57 | Heterogeneity: I2=0, p=0.61 |