

## SUPPLEMENTARY TABLES

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**Suppl. Table 1.** Primers developed for this work

| Polymorphism | Allele-specific forward primers | Reverse primer          |
|--------------|---------------------------------|-------------------------|
| rs1997794    | AACTCGAACTCCCTGGCCCT            | CCTGGAAACGCATCAAAAACCTG |
|              | AACTCGAACTCCCTGGTCCC            |                         |
| rs2235751    | AGCCCTTTCTAGTTGCCGGGA           | CAGTGCTGTCTCAGTGCAGGA   |
|              | AGCCCTTTCTAGTTGCCCGGG           |                         |
| rs6045819    | TAGCGTTTGACAGGTCATCA            | TCCCACGCAGAAGAGAGATA a  |
|              | AGCGTTTGACAGGTCATCG             |                         |

a: from Yuferov *et al.* (2009)

**Suppl. Table 2.** Allele frequencies for the populations extracted from 1000 Genomes Project

| Population | rs1997794 (C) | rs2235751 (A) | rs6045819 (A) | rs10485703 (T) | rs910080 (T) | rs910079 (T) | rs2235749 (C) | rs3808627 (G) | rs6985606 (G) | (n) |
|------------|---------------|---------------|---------------|----------------|--------------|--------------|---------------|---------------|---------------|-----|
| JPT        | 0.798         | 0.226         | 1.000         | 1.000          | 0.255        | 0.255        | 0.255         | 0.625         | 0.668         | 104 |
| MXL        | 0.359         | 0.719         | 0.914         | 0.914          | 0.695        | 0.688        | 0.688         | 0.703         | 0.633         | 64  |
| CEU        | 0.343         | 0.737         | 0.904         | 0.914          | 0.763        | 0.758        | 0.758         | 0.788         | 0.515         | 99  |
| YRI        | 0.875         | 0.269         | 0.611         | 0.806          | 0.537        | 0.523        | 0.523         | 0.991         | 1.000         | 108 |

References: JPT = Japanese in Tokyo; MXL = Mexican ancestry from Los Angeles, California USA; CEU = Residents of Utah with North and Western European ancestry; YRI = Yoruba in Ibadan, Nigeria.




**Suppl. Table 3.** Genotype frequencies of the polymorphisms for the four analysed populations

| Gene             | Polymorphism      | Genotype     | CABA          | La Plata     | Resistencia        | MNP          |
|------------------|-------------------|--------------|---------------|--------------|--------------------|--------------|
| <i>PDYN</i>      | <b>rs35286281</b> | 339/339      | 0.198         | 0.061        | 0.115              | 0.170        |
|                  |                   | 339/407      | 0.321         | 0.394        | 0.438              | 0.528        |
|                  |                   | 339/475      | 0             | 0            | 0.010              | 0            |
|                  |                   | 407/407      | 0.434         | 0.455        | 0.406              | 0.283        |
|                  |                   | 407/475      | 0.028         | 0.030        | 0.021              | 0            |
|                  |                   | 271/339      | 0             | 0.030        | 0                  | 0.019        |
|                  |                   | 271/407      | 0.019         | 0.030        | 0.010              | 0            |
|                  |                   |              | <i>n(106)</i> | <i>n(33)</i> | <i>n(95)</i>       | <i>n(53)</i> |
|                  | <b>rs1997794</b>  | C/C          | 0.236         | 0.212        | 0.156              | 0.185        |
|                  |                   | C/T          | 0.368         | 0.394        | 0.458              | 0.444        |
|                  |                   | T/T          | 0.396         | 0.394        | 0.385              | 0.370        |
|                  |                   |              | <i>n(106)</i> | <i>n(33)</i> | <i>n(95)</i>       | <i>n(54)</i> |
|                  | <b>rs2235751</b>  | A/A          | 0.544         | 0.485        | 0.531              | 0.453        |
|                  |                   | A/G          | 0.262         | 0.394        | 0.375              | 0.434        |
|                  |                   | G/G          | 0.194         | 0.121        | 0.094              | 0.113        |
|                  |                   |              | <i>n(103)</i> | <i>n(33)</i> | <i>n(96)</i>       | <i>n(53)</i> |
|                  | <b>rs6045819</b>  | A/A          | 0.774         | 0.818        | 0.813              | 0.882        |
|                  |                   | A/G          | 0.198         | 0.121        | 0.187              | 0.118        |
|                  |                   | G/G          | 0.028         | 0.061        | 0                  | 0            |
|                  |                   |              | <i>n(106)</i> | <i>n(33)</i> | <i>n(96)</i>       | <i>n(51)</i> |
|                  | <b>rs10485703</b> | C/T          | 0.146         | 0.094        | 0.172              | 0.135        |
|                  |                   | T/T          | 0.854         | 0.906        | 0.828              | 0.865        |
|                  |                   |              | <i>n(82)</i>  | <i>n(32)</i> | <i>n(57)</i>       | <i>n(52)</i> |
|                  | <b>rs910080</b>   | C/C          | 0.172         | 0.031        | 0.040              | 0.140        |
|                  |                   | C/T          | 0.414         | 0.469        | 0.507              | 0.560        |
|                  |                   | T/T          | 0.414         | 0.500        | 0.453              | 0.300        |
|                  |                   |              | <i>n(87)</i>  | <i>n(32)</i> | <i>n(70)</i>       | <i>n(50)</i> |
|                  | <b>rs910079</b>   | C/C          | 0.172         | 0.063        | 0.039              | 0.135        |
| C/T              |                   | 0.403        | 0.406         | 0.500        | 0.538              |              |
| T/T              |                   | 0.425        | 0.531         | 0.461        | 0.327              |              |
|                  |                   | <i>n(87)</i> | <i>n(32)</i>  | <i>n(73)</i> | <i>n(52)</i>       |              |
| <b>rs2235749</b> | C/C               | 0.414        | 0.516         | 0.429        | 0.333              |              |
|                  | C/T               | 0.414        | 0.452         | 0.529        | 0.542              |              |
|                  | T/T               | 0.172        | 0.032         | 0.042        | 0.125              |              |
|                  |                   | <i>n(87)</i> | <i>n(32)</i>  | <i>n(70)</i> | <i>n(48)</i>       |              |
| <i>OPRK1</i>     | <b>rs35566036</b> | del/del      | 0.560         | 0.438        | 0.740 <sup>a</sup> | 0.407        |
|                  |                   | in/del       | 0.380         | 0.438        | 0.240 <sup>a</sup> | 0.519        |
|                  |                   | in/in        | 0.060         | 0.124        | 0.020 <sup>a</sup> | 0.074        |
|                  |                   |              | <i>n(100)</i> | <i>n(32)</i> | <i>n(96)</i>       | <i>n(54)</i> |
|                  | <b>rs3808627</b>  | A/A          | 0.147         | 0.152        | 0.045 <sup>a</sup> | 0.120        |
|                  |                   | A/G          | 0.306         | 0.212        | 0.334 <sup>a</sup> | 0.380        |
|                  |                   | G/G          | 0.547         | 0.636        | 0.621 <sup>a</sup> | 0.500        |
|                  |                   |              | <i>n(95)</i>  | <i>n(33)</i> | <i>n(96)</i>       | <i>n(50)</i> |
|                  | <b>rs6985606</b>  | A/A          | 0.120         | 0.240        | 0.069 <sup>a</sup> | 0.038        |
|                  |                   | A/G          | 0.420         | 0.209        | 0.387 <sup>a</sup> | 0.396        |
|                  |                   | G/G          | 0.460         | 0.551        | 0.544 <sup>a</sup> | 0.566        |
|                  |                   |              | <i>n(100)</i> | <i>n(33)</i> | <i>n(96)</i>       | <i>n(53)</i> |

CABA= Ciudad Autónoma de Buenos Aires; MNP= Misión Nueva Pompeya  
a: data from Raggio et al. (2018)

**Suppl. Table 4.** Linkage Disequilibrium for PDYN and OPRK in CABA, La Plata (LP), Resistencia (RES) and Misión Nueva Pompeya (MNP) respectively. Above the diagonal  $D'$  values, below the diagonal  $r$  values. Values with  $p < 0.01$  are highlighted in red,  $P$  values between 0.01 and 0.05 are highlighted in orange and non significant  $P$  values are highlighted in beige.

| CABA-PDYN  | rs35286281 | rs1997794 | rs2235751 | rs6045819 | rs10485703 | rs910080 | rs910079 | rs2235749 |
|------------|------------|-----------|-----------|-----------|------------|----------|----------|-----------|
| rs35286281 | *          | 0.6881    | 0.6433    | 0.7678    | 0.3661     | 0.4785   | 0.5291   | 0.5291    |
| rs1997794  | 0.6171     | *         | 0.7059    | 0.5465    | 0.7905     | 0.7219   | 0.7562   | 0.7562    |
| rs2235751  | 0.5854     | 0.5761    | *         | 0.9987    | 0.9981     | 0.4959   | 0.5578   | 0.5578    |
| rs6045819  | -0.2238    | 0.2454    | -0.2649   | *         | 0.915      | 0.543    | 0.5178   | 0.5178    |
| rs10485703 | -0.0785    | 0.2611    | -0.1947   | 0.673     | *          | 0.999    | 0.999    | 0.999     |
| rs910080   | 0.4728     | 0.6553    | 0.4459    | 0.2686    | 0.3635     | *        | 0.975    | 0.975     |
| rs910079   | 0.5164     | 0.695     | 0.4954    | 0.253     | 0.3591     | 0.9631   | *        | 0.9997    |
| rs2235749  | 0.5164     | 0.695     | 0.4954    | 0.253     | 0.3591     | 0.9631   | 0.9997   | *         |

  $P < 0.01$   
  $0.01 < P < 0.05$   
  $p > 0.05$

| LP-PDYN    | rs35286281 | rs1997794 | rs2235751 | rs6045819 | rs10485703 | rs910080 | rs910079 | rs2235749 |
|------------|------------|-----------|-----------|-----------|------------|----------|----------|-----------|
| rs35286281 | *          | 0.9048    | 0.5881    | 0.3295    | 0.2725     | 0.5611   | 0.5407   | 0.5989    |
| rs1997794  | 0.717      | *         | 0.8176    | 0.7529    | 0.9982     | 0.8994   | 0.8954   | 0.8741    |
| rs2235751  | 0.5677     | 0.6712    | *         | 0.1205    | 0.2086     | 0.5557   | 0.5338   | 0.4486    |
| rs6045819  | 0.1856     | 0.3361    | 0.0655    | *         | 0.9988     | 0.3952   | 0.3952   | 0.41      |
| rs10485703 | 0.0917     | 0.2661    | 0.0677    | 0.5964    | *          | 0.9986   | 0.9986   | 0.9986    |
| rs910080   | 0.5118     | 0.6501    | 0.4892    | 0.244     | 0.3682     | *        | 0.833    | 0.7988    |
| rs910079   | 0.4931     | 0.6472    | 0.4699    | 0.244     | 0.3682     | 0.833    | *        | 0.997     |
| rs2235749  | 0.5356     | 0.6196    | 0.3873    | 0.2582    | 0.3755     | 0.7833   | 0.9777   | *         |

| RES-PDYN   | rs35286281 | rs1997794 | rs2235751 | rs6045819 | rs10485703 | rs910080 | rs910079 | rs2235749 |
|------------|------------|-----------|-----------|-----------|------------|----------|----------|-----------|
| rs35286281 | *          | 0.7104    | 0.8159    | 0.5638    | 0.9979     | 0.3959   | 0.4096   | 0.4143    |
| rs1997794  | 0.6363     | *         | 0.7055    | 0.7589    | 0.7846     | 0.6257   | 0.6306   | 0.5939    |
| rs2235751  | 0.7134     | 0.5526    | *         | 0.5506    | 0.9975     | 0.4837   | 0.4784   | 0.508     |
| rs6045819  | -0.1297    | 0.3056    | -0.1108   | *         | 0.8095     | 0.8657   | 0.8545   | 0.8473    |
| rs10485703 | -0.2193    | 0.3017    | -0.1916   | 0.773     | *          | 0.999    | 0.999    | 0.999     |
| rs910080   | 0.3533     | 0.5       | 0.474     | 0.4362    | 0.4807     | *        | 0.9996   | 0.9996    |
| rs910079   | 0.3639     | 0.5018    | 0.4709    | 0.4325    | 0.4828     | 0.9952   | *        | 0.9996    |
| rs2235749  | 0.3856     | 0.4951    | 0.4773    | 0.4093    | 0.4608     | 0.9583   | 0.9541   | *         |

| MNP-PDYN   | rs35286281 | rs1997794 | rs2235751 | rs6045819 | rs10485703 | rs910080 | rs910079 | rs2235749 |
|------------|------------|-----------|-----------|-----------|------------|----------|----------|-----------|
| rs35286281 | *          | 0.7097    | 0.737     | 0.4238    | 0.4069     | 0.697    | 0.6594   | 0.7153    |
| rs1997794  | 0.6468     | *         | 0.7245    | 0.998     | 0.998      | 0.8187   | 0.8211   | 0.8141    |
| rs2235751  | 0.5688     | 0.6135    | *         | 0.0002    | 0.9964     | 0.8231   | 0.8277   | 0.8048    |
| rs6045819  | 0.1165     | 0.3009    | 0         | *         | 0.8608     | 0.998    | 0.998    | 0.998     |
| rs10485703 | -0.0994    | 0.3233    | -0.1879   | 0.8011    | *          | 0.998    | 0.998    | 0.998     |
| rs910080   | 0.6306     | 0.8127    | 0.7022    | 0.3031    | 0.3257     | *        | 0.9997   | 0.9997    |
| rs910079   | 0.6168     | 0.8       | 0.6829    | 0.2932    | 0.315      | 0.9669   | *        | 0.9997    |
| rs2235749  | 0.6365     | 0.7948    | 0.6981    | 0.3083    | 0.3312     | 0.9832   | 0.9509   | *         |

| <b>CABA-OPRK</b> | <b>rs35566036</b> | <b>rs3808627</b> | <b>rs6985606</b> |
|------------------|-------------------|------------------|------------------|
| rs35566036       | *                 | 0.8278           | 0.9992           |
| rs3808627        | -0.3129           | *                | 0.7887           |
| rs6985606        | -0.4048           | -0.3623          | *                |

| <b>LP-OPRK</b> | <b>rs35566036</b> | <b>rs3808627</b> | <b>rs6985606</b> |
|----------------|-------------------|------------------|------------------|
| rs35566036     | *                 | 0.3645           | 0.9995           |
| rs3808627      | -0.1554           | *                | 0.9992           |
| rs6985606      | -0.5291           | -0.4304          | *                |

| <b>RES-OPRK</b> | <b>rs35566036</b> | <b>rs3808627</b> | <b>rs6985606</b> |
|-----------------|-------------------|------------------|------------------|
| rs35566036      | *                 | 0.9981           | 0.5604           |
| rs3808627       | -0.1859           | *                | 0.2503           |
| rs6985606       | -0.1343           | -0.0821          | *                |

| <b>MNP-OPRK</b> | <b>rs35566036</b> | <b>rs3808627</b> | <b>rs6985606</b> |
|-----------------|-------------------|------------------|------------------|
| rs35566036      | *                 | 0.8536           | 0.9992           |
| rs3808627       | -0.4046           | *                | 0.7483           |
| rs6985606       | -0.3925           | -0.2786          | *                |