

**Table S2A. Detailed summary statistics of Functional Enrichment Analysis within Runs of Homozygosity (ROH) Islands. This table presents the detailed statistics of functional enrichment analysis on genes identified within runs of homozygosity (ROH) islands (> 100 KB), detected in the BirThree dataset via BCFtools (by setting 99.9<sup>th</sup> percentile threshold based on the frequencies of overlapping ROH<sub>100</sub> regions shared among individuals). The gProfiler tool was utilized to identify enriched biological pathways (BP), molecular functions (MF), and cellular components (CC) from Gene Ontology (GO), KEGG, and Reactome. The intersections column displays the genes from the query list that overlap with each functional term, contributing to its statistical significance. Detailed information regarding statistics can be found on gProfiler website.**

| source | term_name                                 | term_id    | highlighted | adjusted_p_value | negative_log10_of_adjusted_p_value | term_size | query_size | intersection_size | effective_domain_size | intersections                                                                                                                                                                   |
|--------|-------------------------------------------|------------|-------------|------------------|------------------------------------|-----------|------------|-------------------|-----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| GO:MF  | cysteine-type deubiquitinase activity     | GO:0004843 | TRUE        | 1.05E-26         | 25.97906294                        | 117       | 68         | 20                | 20212                 | USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L23,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5,USP38 |
| GO:MF  | deubiquitinase activity                   | GO:0101005 | FALSE       | 3.08E-26         | 25.51195338                        | 123       | 68         | 20                | 20212                 | USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L23,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5,USP38 |
| GO:MF  | ubiquitin-like protein peptidase activity | GO:0019783 | FALSE       | 1.92E-25         | 24.71745951                        | 134       | 68         | 20                | 20212                 | USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L23,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5,USP38 |
| GO:MF  | cysteine-type peptidase activity          | GO:0008234 | FALSE       | 6.72E-22         | 21.1727389                         | 198       | 68         | 20                | 20212                 | USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L23,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5,USP38 |

|       |                                               |            |       |             |             |      |    |    |       |                                                                                                                                                                                                          |
|-------|-----------------------------------------------|------------|-------|-------------|-------------|------|----|----|-------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| GO:MF | peptidase activity                            | GO:0008233 | FALSE | 4.81E-12    | 11.31803605 | 625  | 68 | 20 | 20212 | USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L23,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5,USP38                          |
| GO:MF | bitter taste receptor activity                | GO:0033038 | TRUE  | 1.32E-10    | 9.880732468 | 20   | 68 | 7  | 20212 | TAS2R14,TAS2R20,TAS2R30,TAS2R31,TAS2R43,TAS2R46,TAS2R50                                                                                                                                                  |
| GO:MF | taste receptor activity                       | GO:0008527 | FALSE | 1.10E-09    | 8.958945242 | 26   | 68 | 7  | 20212 | TAS2R14,TAS2R20,TAS2R30,TAS2R31,TAS2R43,TAS2R46,TAS2R50                                                                                                                                                  |
| GO:MF | hyaluronic acid binding                       | GO:0005540 | TRUE  | 3.19E-07    | 6.495946904 | 30   | 68 | 6  | 20212 | USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30                                                                                                                                                    |
| GO:MF | hydrolase activity                            | GO:0016787 | FALSE | 0.000391363 | 3.407419945 | 2478 | 68 | 24 | 20212 | ATAD5,INPP4B,LARS1,PSMC4,USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L23,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5,USP38 |
| GO:MF | catalytic activity, acting on a protein       | GO:0140096 | FALSE | 0.002472606 | 2.606845145 | 2355 | 68 | 22 | 20212 | RANBP2,SH3RF2,USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L23,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5,USP38            |
| GO:BP | protein deubiquitination                      | GO:0016579 | TRUE  | 4.90E-26    | 25.31021184 | 125  | 67 | 20 | 21031 | USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L23,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5,USP38                          |
| GO:BP | protein modification by small protein removal | GO:0070646 | FALSE | 6.37E-25    | 24.19574    | 141  | 67 | 20 | 21031 | USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L23,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5,USP38                          |

|       |                                                                                    |            |       |            |             |      |    |    |       |                                                                                                                                                                                                     |
|-------|------------------------------------------------------------------------------------|------------|-------|------------|-------------|------|----|----|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| GO:BP | protein modification by small protein conjugation or removal                       | GO:0070647 | FALSE | 1.90E-11   | 10.72071432 | 970  | 67 | 23 | 21031 | RANBP2,SH3RF2,SPSB4,USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L23,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5,USP38 |
| GO:BP | post-translational protein modification                                            | GO:0043687 | FALSE | 5.63E-11   | 10.24951294 | 1021 | 67 | 23 | 21031 | RANBP2,SH3RF2,SPSB4,USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L23,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5,USP38 |
| GO:BP | protein deubiquitination involved in ubiquitin-dependent protein catabolic process | GO:0071947 | FALSE | 2.98E-10   | 9.52593954  | 10   | 67 | 6  | 21031 | USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30                                                                                                                                               |
| GO:BP | sensory perception of taste                                                        | GO:0050909 | TRUE  | 1.23E-09   | 8.909289075 | 67   | 67 | 9  | 21031 | TAS2R14,TAS2R19,TAS2R20,TAS2R30,TAS2R31,TAS2R42,TAS2R43,TAS2R46,TAS2R50                                                                                                                             |
| GO:BP | detection of chemical stimulus involved in sensory perception of bitter taste      | GO:0001580 | FALSE | 3.97E-08   | 7.401170044 | 37   | 67 | 7  | 21031 | TAS2R14,TAS2R20,TAS2R30,TAS2R31,TAS2R43,TAS2R46,TAS2R50                                                                                                                                             |
| GO:BP | sensory perception of bitter taste                                                 | GO:0050913 | FALSE | 1.03E-07   | 6.988230919 | 42   | 67 | 7  | 21031 | TAS2R14,TAS2R20,TAS2R30,TAS2R31,TAS2R43,TAS2R46,TAS2R50                                                                                                                                             |
| GO:BP | detection of chemical stimulus involved in sensory perception of taste             | GO:0050912 | FALSE | 1.22E-07   | 6.912150899 | 43   | 67 | 7  | 21031 | TAS2R14,TAS2R20,TAS2R30,TAS2R31,TAS2R43,TAS2R46,TAS2R50                                                                                                                                             |
| GO:BP | proteolysis                                                                        | GO:0006508 | TRUE  | 2.5598E-06 | 5.591793263 | 1573 | 67 | 22 | 21031 | PSMC4,SH3RF2,SPSB4,USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5,USP38           |

|       |                                                          |            |       |             |             |      |    |    |       |                                                                                                                                                                                    |
|-------|----------------------------------------------------------|------------|-------|-------------|-------------|------|----|----|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| GO:BP | positive regulation of epithelial cell apoptotic process | GO:1904037 | TRUE  | 6.87156E-06 | 5.162944682 | 42   | 67 | 6  | 21031 | USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30                                                                                                                              |
| GO:BP | regulation of apoptotic process                          | GO:0042981 | FALSE | 2.61927E-05 | 4.581820448 | 1463 | 67 | 20 | 21031 | ATAD5,SH3RF2,USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5      |
| GO:BP | regulation of programmed cell death                      | GO:0043067 | FALSE | 4.25743E-05 | 4.370852427 | 1506 | 67 | 20 | 21031 | ATAD5,SH3RF2,USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5      |
| GO:BP | apoptotic process                                        | GO:0006915 | FALSE | 0.000450639 | 3.346171422 | 1913 | 67 | 21 | 21031 | ATAD5,EDAR,SH3RF2,USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5 |
| GO:BP | programmed cell death                                    | GO:0012501 | FALSE | 0.000828002 | 3.081968606 | 1984 | 67 | 21 | 21031 | ATAD5,EDAR,SH3RF2,USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5 |
| GO:BP | cell death                                               | GO:0008219 | FALSE | 0.000856152 | 3.06744928  | 1988 | 67 | 21 | 21031 | ATAD5,EDAR,SH3RF2,USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5 |
| GO:BP | regulation of epithelial cell apoptotic process          | GO:1904035 | FALSE | 0.002368975 | 2.62543956  | 110  | 67 | 6  | 21031 | USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30                                                                                                                              |
| GO:BP | epithelial cell apoptotic process                        | GO:1904019 | FALSE | 0.009630749 | 2.016339933 | 140  | 67 | 6  | 21031 | USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30                                                                                                                              |

|       |                                                        |            |       |                 |             |      |    |    |       |                                                                                                                                                                                                                                                                                 |
|-------|--------------------------------------------------------|------------|-------|-----------------|-------------|------|----|----|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| GO:BP | protein modification process                           | GO:0036211 | FALSE | 0.018015<br>379 | 1.744356603 | 3031 | 67 | 24 | 21031 | ERC1,RANBP2,SH3RF2,SPSB4,USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L23,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5,USP38                                                                        |
| GO:BP | macromolecule modification                             | GO:0043412 | FALSE | 0.019219<br>394 | 1.716260303 | 3262 | 67 | 25 | 21031 | ARID4B,ERC1,RANBP2,SH3RF2,SPSB4,USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L23,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5,USP38                                                                 |
| GO:BP | ubiquitin-dependent protein catabolic process          | GO:0006511 | FALSE | 0.032324<br>563 | 1.490467333 | 599  | 67 | 10 | 21031 | PSMC4,SH3RF2,SPSB4,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP38                                                                                                                                                                                                  |
| GO:BP | modification-dependent protein catabolic process       | GO:0019941 | FALSE | 0.037250<br>46  | 1.428868364 | 609  | 67 | 10 | 21031 | PSMC4,SH3RF2,SPSB4,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP38                                                                                                                                                                                                  |
| GO:BP | modification-dependent macromolecule catabolic process | GO:0043632 | FALSE | 0.043402<br>72  | 1.362483053 | 620  | 67 | 10 | 21031 | PSMC4,SH3RF2,SPSB4,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP38                                                                                                                                                                                                  |
| GO:BP | sensory perception of chemical stimulus                | GO:0007606 | FALSE | 0.046685<br>693 | 1.330816191 | 497  | 67 | 9  | 21031 | TAS2R14,TAS2R19,TAS2R20,TAS2R30,TAS2R31,TAS2R42,TAS2R43,TAS2R46,TAS2R50                                                                                                                                                                                                         |
| GO:CC | endoplasmic reticulum                                  | GO:0005783 | TRUE  | 0.000100<br>46  | 3.998007029 | 2055 | 67 | 21 | 22097 | LARS1,PLN,USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L23,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5                                                                                             |
| GO:CC | cytosol                                                | GO:0005829 | TRUE  | 0.001139<br>431 | 2.943312076 | 5487 | 67 | 34 | 22097 | AKAP10,ARID4B,CLASP1,CRLF3,ERC1,GGC2,GGPS1,INPP4B,LARS1,LIMS1,PSMC4,RANBP2,SPECC1,SPSB4,SULT1C4,USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L23,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5,USP38 |

|      |                                                                  |                    |       |             |             |      |    |    |       |                                                                                                                                                                                                           |
|------|------------------------------------------------------------------|--------------------|-------|-------------|-------------|------|----|----|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| KEGG | Taste transduction                                               | KEGG:04742         | TRUE  | 1.13E-11    | 10.94662962 | 85   | 21 | 9  | 8484  | TAS2R14,TAS2R19,TAS2R20,TAS2R30,TAS2R31,TAS2R42,TAS2R43,TAS2R46,TAS2R50                                                                                                                                   |
| REAC | Ub-specific processing proteases                                 | REAC:R-HSA-5689880 | TRUE  | 1.15E-18    | 17.93943936 | 221  | 44 | 19 | 10842 | PSMC4,USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5                                    |
| REAC | Deubiquitination                                                 | REAC:R-HSA-5688426 | TRUE  | 3.28E-16    | 15.48406807 | 297  | 44 | 19 | 10842 | PSMC4,USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5                                    |
| REAC | Class C/3 (Metabotropic glutamate/pheromone receptors)           | REAC:R-HSA-420499  | FALSE | 8.97E-12    | 11.04734743 | 39   | 44 | 9  | 10842 | TAS2R14,TAS2R19,TAS2R20,TAS2R30,TAS2R31,TAS2R42,TAS2R43,TAS2R46,TAS2R50                                                                                                                                   |
| REAC | Sensory perception of sweet, bitter, and umami (glutamate) taste | REAC:R-HSA-9717207 | TRUE  | 8.26E-08    | 7.082803785 | 41   | 44 | 7  | 10842 | TAS2R14,TAS2R20,TAS2R30,TAS2R31,TAS2R43,TAS2R46,TAS2R50                                                                                                                                                   |
| REAC | Sensory perception of taste                                      | REAC:R-HSA-9717189 | TRUE  | 2.27E-07    | 6.643852968 | 47   | 44 | 7  | 10842 | TAS2R14,TAS2R20,TAS2R30,TAS2R31,TAS2R43,TAS2R46,TAS2R50                                                                                                                                                   |
| REAC | Post-translational protein modification                          | REAC:R-HSA-597592  | FALSE | 9.10831E-06 | 5.040562068 | 1419 | 44 | 21 | 10842 | PSMC4,RANBP2,SPSB4,USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5                       |
| REAC | Metabolism of proteins                                           | REAC:R-HSA-392499  | FALSE | 9.361E-05   | 4.028677871 | 1946 | 44 | 23 | 10842 | ENSG00000285053,LARS1,PSMC4,RANBP2,SPSB4,USP17L10,USP17L11,USP17L12,USP17L13,USP17L15,USP17L17,USP17L18,USP17L19,USP17L20,USP17L21,USP17L22,USP17L24,USP17L26,USP17L27,USP17L28,USP17L29,USP17L30,USP17L5 |

|      |                               |                   |       |                 |             |     |    |   |       |                                                                         |
|------|-------------------------------|-------------------|-------|-----------------|-------------|-----|----|---|-------|-------------------------------------------------------------------------|
| REAC | G alpha (i) signalling events | REAC:R-HSA-418594 | FALSE | 0.001303<br>905 | 2.884754075 | 312 | 44 | 9 | 10842 | TAS2R14,TAS2R19,TAS2R20,TAS2R30,TAS2R31,TAS2R42,TAS2R43,TAS2R46,TAS2R50 |
| REAC | GPCR ligand binding           | REAC:R-HSA-500792 | FALSE | 0.028723<br>338 | 1.541765097 | 460 | 44 | 9 | 10842 | TAS2R14,TAS2R19,TAS2R20,TAS2R30,TAS2R31,TAS2R42,TAS2R43,TAS2R46,TAS2R50 |

**Table S2B. Detailed summary statistics of Functional Enrichment Analysis within Runs of Homozygosity (ROH) Islands. This table presents the detailed statistics of functional enrichment analysis on genes identified within runs of homozygosity (ROH) islands (> 100 KB), detected in the BirThree dataset via PLINK (by setting 99.9<sup>th</sup> percentile threshold based on the frequencies of overlapping ROH<sub>100</sub> regions shared among individuals). The gProfiler tool was utilized to identify enriched biological pathways (BP), molecular functions (MF), and cellular components (CC) from Gene Ontology (GO), KEGG, and Reactome. The intersections column displays the genes from the query list that overlap with each functional term, contributing to its statistical significance. Detailed information regarding statistics can be found on gProfiler website.**

| source | term_name                                                   | term_id    | highlighted | adjusted_p_value | negative_log10_of_adjusted_p_value | term_size | query_size | intersection_size | effective_domain_size | intersections          |
|--------|-------------------------------------------------------------|------------|-------------|------------------|------------------------------------|-----------|------------|-------------------|-----------------------|------------------------|
| GO:MF  | 3-hydroxyacyl-CoA dehydrogenase activity                    | GO:0003857 | TRUE        | 0.002935338      | 2.532341826                        | 7         | 105        | 3                 | 20212                 | HADHA,HADHB,HSD17B12   |
| GO:MF  | cysteine desulfurase activity                               | GO:0031071 | TRUE        | 0.016707273      | 1.777094436                        | 2         | 105        | 2                 | 20212                 | ENSG00000272897,NFS1   |
| GO:MF  | long-chain-3-hydroxyacyl-CoA dehydrogenase activity         | GO:0016509 | FALSE       | 0.049951522      | 1.301451278                        | 3         | 105        | 2                 | 20212                 | HADHA,HSD17B12         |
| GO:MF  | vitamin-K-epoxide reductase (warfarin-sensitive) activity   | GO:0047057 | TRUE        | 0.049951522      | 1.301451278                        | 3         | 105        | 2                 | 20212                 | ENSG00000255439,VKORC1 |
| GO:CC  | mitochondrial fatty acid beta-oxidation multienzyme complex | GO:0016507 | TRUE        | 0.024690922      | 1.607462701                        | 3         | 109        | 2                 | 22097                 | HADHA,HADHB            |
| GO:CC  | fatty acid beta-oxidation multienzyme complex               | GO:0036125 | FALSE       | 0.024690922      | 1.607462701                        | 3         | 109        | 2                 | 22097                 | HADHA,HADHB            |

|      |                                                  |                  |       |             |             |    |    |   |       |                      |
|------|--------------------------------------------------|------------------|-------|-------------|-------------|----|----|---|-------|----------------------|
| KEGG | Fatty acid elongation                            | KEGG:00062       | TRUE  | 0.009873472 | 2.005530103 | 27 | 32 | 3 | 8484  | HADHA,HADHB,HSD17B12 |
| REAC | Beta oxidation of myristoyl-CoA to lauroyl-CoA   | REAC:R-HSA-77285 | TRUE  | 0.025043751 | 1.60130063  | 3  | 53 | 2 | 10842 | HADHA,HADHB          |
| REAC | Beta oxidation of palmitoyl-CoA to myristoyl-CoA | REAC:R-HSA-77305 | FALSE | 0.025043751 | 1.60130063  | 3  | 53 | 2 | 10842 | HADHA,HADHB          |

**Table S2C. Detailed summary statistics of Functional Enrichment Analysis within Runs of Homozygosity (ROH) Islands.** This table presents the detailed statistics of functional enrichment analysis on genes identified within runs of homozygosity (ROH) islands (> 100 KB), detected in the 3.5KJPNv2 dataset via PLINK (by setting 99.9<sup>th</sup> percentile threshold based on the frequencies of overlapping ROH<sub>100</sub> regions shared among individuals). The gProfiler tool was utilized to identify enriched biological pathways (BP), molecular functions (MF), and cellular components (CC) from Gene Ontology (GO), KEGG, and Reactome. The intersections column displays the genes from the query list that overlap with each functional term, contributing to its statistical significance. Detailed information regarding statistics can be found on gProfiler website.

| source | term_name                                                 | term_id    | highlighted | adjusted_p_value | negative_log10_of_adjusted_p_value | term_size | query_size | intersection_size | effective_domain_size | intersections          |
|--------|-----------------------------------------------------------|------------|-------------|------------------|------------------------------------|-----------|------------|-------------------|-----------------------|------------------------|
| GO:MF  | vitamin-K-epoxide reductase (warfarin-sensitive) activity | GO:0047057 | TRUE        | 0.049953         | 1.301437                           | 3         | 101        | 2                 | 20212                 | ENSG00000255439,VKORC1 |

**Table S2D. Detailed summary statistics of Functional Enrichment Analysis within Runs of Homozygosity (ROH) Islands. This table presents the detailed statistics of functional enrichment analysis on genes identified within runs of homozygosity (ROH) islands (> 1.5 MB), detected in the BirThree dataset via BCFtools (by setting 99.5<sup>th</sup> percentile threshold based on the frequencies of overlapping ROH<sub>1500</sub> regions shared among individuals). The gProfiler tool was utilized to identify enriched biological pathways (BP), molecular functions (MF), and cellular components (CC) from Gene Ontology (GO), KEGG, and Reactome. The intersections column displays the genes from the query list that overlap with each functional term, contributing to its statistical significance. Detailed information regarding statistics can be found on gProfiler website.**

| source | term_name                                                              | term_id     | highlighted | adjusted_p_value | negative_log10_of_adjusted_p_value | term_size | query_size | intersection_size | effective_dominant_size | intersections                                            |
|--------|------------------------------------------------------------------------|-------------|-------------|------------------|------------------------------------|-----------|------------|-------------------|-------------------------|----------------------------------------------------------|
| GO:MF  | olfactory receptor activity                                            | GO:0004984  | TRUE        | 8.17E-09         | 8.087860736                        | 397       | 19         | 9                 | 20212                   | OR4A47,OR4B1,OR4C12,OR4C13,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| GO:MF  | G protein-coupled receptor activity                                    | GO:0004930  | FALSE       | 5.83018E-06      | 5.234318358                        | 838       | 19         | 9                 | 20212                   | OR4A47,OR4B1,OR4C12,OR4C13,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| GO:MF  | transmembrane signaling receptor activity                              | GO:0004888  | FALSE       | 0.000202748      | 3.69304294                         | 1269      | 19         | 9                 | 20212                   | OR4A47,OR4B1,OR4C12,OR4C13,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| GO:MF  | molecular transducer activity                                          | GO:0006089  | FALSE       | 0.000782508      | 3.10651107                         | 1491      | 19         | 9                 | 20212                   | OR4A47,OR4B1,OR4C12,OR4C13,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| GO:MF  | signaling receptor activity                                            | GO:00038023 | FALSE       | 0.000782508      | 3.10651107                         | 1491      | 19         | 9                 | 20212                   | OR4A47,OR4B1,OR4C12,OR4C13,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| GO:BP  | detection of chemical stimulus involved in sensory perception of smell | GO:00050911 | TRUE        | 8.70E-09         | 8.060442621                        | 397       | 17         | 9                 | 21031                   | OR4A47,OR4B1,OR4C12,OR4C13,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| GO:BP  | sensory perception of smell                                            | GO:00007608 | FALSE       | 1.53E-08         | 7.813969769                        | 423       | 17         | 9                 | 21031                   | OR4A47,OR4B1,OR4C12,OR4C13,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| GO:BP  | detection of chemical stimulus involved in sensory perception          | GO:00050907 | FALSE       | 2.32E-08         | 7.634734984                        | 443       | 17         | 9                 | 21031                   | OR4A47,OR4B1,OR4C12,OR4C13,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| GO:BP  | detection of chemical stimulus                                         | GO:00009593 | FALSE       | 4.74E-08         | 7.324048079                        | 480       | 17         | 9                 | 21031                   | OR4A47,OR4B1,OR4C12,OR4C13,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| GO:BP  | sensory perception of chemical stimulus                                | GO:00007606 | FALSE       | 6.46E-08         | 7.1894626                          | 497       | 17         | 9                 | 21031                   | OR4A47,OR4B1,OR4C12,OR4C13,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| GO:BP  | detection of stimulus involved in sensory perception                   | GO:00050906 | FALSE       | 8.87E-08         | 7.052024764                        | 515       | 17         | 9                 | 21031                   | OR4A47,OR4B1,OR4C12,OR4C13,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| GO:BP  | detection of stimulus                                                  | GO:00051606 | FALSE       | 6.61E-07         | 6.179920045                        | 646       | 17         | 9                 | 21031                   | OR4A47,OR4B1,OR4C12,OR4C13,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |

|       |                                                     |                    |       |             |             |      |    |   |       |                                                          |
|-------|-----------------------------------------------------|--------------------|-------|-------------|-------------|------|----|---|-------|----------------------------------------------------------|
| GO:BP | sensory perception                                  | GO:0007600         | FALSE | 1.99769E-05 | 4.699471336 | 953  | 17 | 9 | 21031 | OR4A47,OR4B1,OR4C12,OR4C13,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| GO:BP | G protein-coupled receptor signaling pathway        | GO:0007186         | TRUE  | 0.000256936 | 3.590175775 | 1281 | 17 | 9 | 21031 | OR4A47,OR4B1,OR4C12,OR4C13,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| GO:BP | nervous system process                              | GO:0050877         | FALSE | 0.000900599 | 3.045468541 | 1484 | 17 | 9 | 21031 | OR4A47,OR4B1,OR4C12,OR4C13,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| GO:BP | system process                                      | GO:0003008         | FALSE | 0.029819408 | 1.525500978 | 2258 | 17 | 9 | 21031 | OR4A47,OR4B1,OR4C12,OR4C13,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| KEGG  | Olfactory transduction                              | KEGG:04740         | TRUE  | 1.14E-09    | 8.941297157 | 428  | 10 | 9 | 8484  | OR4A47,OR4B1,OR4C12,OR4C13,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| REAC  | Expression and translocation of olfactory receptors | REAC:R-HSA-9752946 | TRUE  | 1.02E-10    | 9.991767365 | 354  | 10 | 9 | 10842 | OR4A47,OR4B1,OR4C12,OR4C13,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| REAC  | Olfactory Signaling Pathway                         | REAC:R-HSA-381753  | TRUE  | 1.22E-10    | 9.914621786 | 361  | 10 | 9 | 10842 | OR4A47,OR4B1,OR4C12,OR4C13,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| REAC  | Sensory Perception                                  | REAC:R-HSA-9709957 | TRUE  | 8.19E-09    | 8.086876154 | 575  | 10 | 9 | 10842 | OR4A47,OR4B1,OR4C12,OR4C13,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |

**Table S2E. Detailed summary statistics of Functional Enrichment Analysis within Runs of Homozygosity (ROH) Islands. This table presents the detailed statistics of functional enrichment analysis on genes identified within runs of homozygosity (ROH) islands (> 1.5 MB), detected in the 3.5KJPNv2 dataset via BCFtools (by setting 99.5<sup>th</sup> percentile threshold based on the frequencies of overlapping ROH<sub>1500</sub> regions shared among individuals). The gProfiler tool was utilized to identify enriched biological pathways (BP), molecular functions (MF), and cellular components (CC) from Gene Ontology (GO), KEGG, and Reactome. The intersections column displays the genes from the query lists that overlap with each functional term, contributing to its statistical significance. Detailed information regarding statistics can be found on gProfiler website.**

| source | term_name                                                              | term_id    | highlighted | adjusted_p_value | negative_log10_of_adjusted_p_value | term_size | query_size | intersection_size | effective_domain_size | intersections                                    |
|--------|------------------------------------------------------------------------|------------|-------------|------------------|------------------------------------|-----------|------------|-------------------|-----------------------|--------------------------------------------------|
| GO: MF | olfactory receptor activity                                            | GO:0004984 | TRUE        | 1.16359E-05      | 4.934201324                        | 397       | 19         | 7                 | 20212                 | OR4A47,OR4B1,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2       |
| GO: MF | G protein-coupled receptor activity                                    | GO:0004930 | FALSE       | 0.001767715      | 2.752587866                        | 838       | 19         | 7                 | 20212                 | OR4A47,OR4B1,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2       |
| GO: MF | transmembrane signaling receptor activity                              | GO:0004888 | FALSE       | 0.025801957      | 1.58834736                         | 1269      | 19         | 7                 | 20212                 | OR4A47,OR4B1,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2       |
| GO: BP | detection of chemical stimulus involved in sensory perception of smell | GO:0050911 | TRUE        | 4.79621E-05      | 4.319101915                        | 397       | 19         | 7                 | 21031                 | OR4A47,OR4B1,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2       |
| GO: BP | detection of stimulus                                                  | GO:0051606 | FALSE       | 6.07501E-05      | 4.216453048                        | 646       | 19         | 8                 | 21031                 | OR4A47,OR4B1,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2,PTPRJ |
| GO: BP | sensory perception of smell                                            | GO:0007608 | FALSE       | 7.40381E-05      | 4.130545027                        | 423       | 19         | 7                 | 21031                 | OR4A47,OR4B1,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2       |

|           |                                                               |                    |       |             |             |     |    |   |       |                                            |
|-----------|---------------------------------------------------------------|--------------------|-------|-------------|-------------|-----|----|---|-------|--------------------------------------------|
| GO:<br>BP | detection of chemical stimulus involved in sensory perception | GO:0050907         | FALSE | 0.000101503 | 3.993521188 | 443 | 19 | 7 | 21031 | OR4A47,OR4B1,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| GO:<br>BP | detection of chemical stimulus                                | GO:0009593         | FALSE | 0.000175303 | 3.756209969 | 480 | 19 | 7 | 21031 | OR4A47,OR4B1,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| GO:<br>BP | sensory perception of chemical stimulus                       | GO:0007606         | FALSE | 0.000222076 | 3.65349779  | 497 | 19 | 7 | 21031 | OR4A47,OR4B1,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| GO:<br>BP | detection of stimulus involved in sensory perception          | GO:0050906         | FALSE | 0.000282704 | 3.548667552 | 515 | 19 | 7 | 21031 | OR4A47,OR4B1,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| GO:<br>BP | sensory perception                                            | GO:0007600         | FALSE | 0.01710409  | 1.766900033 | 953 | 19 | 7 | 21031 | OR4A47,OR4B1,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| KEG<br>G  | Olfactory transduction                                        | KEGG:04740         | TRUE  | 5.11334E-06 | 5.291295137 | 428 | 10 | 7 | 8484  | OR4A47,OR4B1,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| REA<br>C  | Expression and translocation of olfactory receptors           | REAC:R-HSA-9752946 | TRUE  | 7.50245E-06 | 5.124796741 | 354 | 12 | 7 | 10842 | OR4A47,OR4B1,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| REA<br>C  | Olfactory Signaling Pathway                                   | REAC:R-HSA-381753  | TRUE  | 8.58965E-06 | 5.066024533 | 361 | 12 | 7 | 10842 | OR4A47,OR4B1,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |
| REA<br>C  | Sensory Perception                                            | REAC:R-HSA-9709957 | TRUE  | 0.00020879  | 3.680290025 | 575 | 12 | 7 | 10842 | OR4A47,OR4B1,OR4C3,OR4C5,OR4S1,OR4X1,OR4X2 |

**Table S2F. Detailed summary statistics of Functional Enrichment Analysis within Runs of Homozygosity (ROH) Islands. This table presents the detailed statistics of functional enrichment analysis on genes identified within runs of homozygosity (ROH) islands (> 1.5 MB), detected in the 3.5KJPNv2 dataset via PLINK (by setting 99.5<sup>th</sup> percentile threshold based on the frequencies of overlapping ROH<sub>1500</sub> regions shared among individuals). The gProfiler tool was utilized to identify enriched biological pathways (BP), molecular functions (MF), and cellular components (CC) from Gene Ontology (GO), KEGG, and Reactome. The intersections column displays the genes from the query list that overlap with each functional term, contributing to its statistical significance. Detailed information regarding statistics can be found on gProfiler website.**

| source    | term_name                                                  | term_id            | highlighted | adjusted_p_value | negative_log10_of_adjusted_p_value | term_size | query_size | intersection_size | effective_domain_size | intersections          |
|-----------|------------------------------------------------------------|--------------------|-------------|------------------|------------------------------------|-----------|------------|-------------------|-----------------------|------------------------|
| GO:<br>MF | aminomethyltransferase activity                            | GO:0004047         | TRUE        | 0.010263084      | 1.988722098                        | 3         | 56         | 2                 | 20212                 | AMT,ENSG00000283189    |
| GO:<br>MF | inositol 5-diphosphate pentakisphosphate 5-kinase activity | GO:0052836         | TRUE        | 0.010263084      | 1.988722098                        | 3         | 56         | 2                 | 20212                 | IP6K1,IP6K2            |
| GO:<br>MF | inositol diphosphate tetrakisphosphate kinase activity     | GO:0052839         | TRUE        | 0.010263084      | 1.988722098                        | 3         | 56         | 2                 | 20212                 | IP6K1,IP6K2            |
| GO:<br>MF | IMP dehydrogenase activity                                 | GO:0003938         | TRUE        | 0.020489612      | 1.688466255                        | 4         | 56         | 2                 | 20212                 | ENSG00000290315,IMPDH2 |
| GO:<br>MF | inositol-1,3,4,5,6-pentakisphosphate kinase activity       | GO:0000827         | TRUE        | 0.034088547      | 1.467391515                        | 5         | 56         | 2                 | 20212                 | IP6K1,IP6K2            |
| GO:<br>MF | inositol hexakisphosphate kinase activity                  | GO:0000828         | FALSE       | 0.034088547      | 1.467391515                        | 5         | 56         | 2                 | 20212                 | IP6K1,IP6K2            |
| GO:<br>MF | inositol heptakisphosphate kinase activity                 | GO:0000829         | TRUE        | 0.034088547      | 1.467391515                        | 5         | 56         | 2                 | 20212                 | IP6K1,IP6K2            |
| GO:<br>MF | inositol hexakisphosphate 5-kinase activity                | GO:0000832         | TRUE        | 0.034088547      | 1.467391515                        | 5         | 56         | 2                 | 20212                 | IP6K1,IP6K2            |
| REAC      | Synthesis of IPs in the nucleus                            | REAC:R-HSA-1855191 | TRUE        | 0.020033096      | 1.698251925                        | 4         | 35         | 2                 | 10842                 | IP6K1,IP6K2            |