**Supplementary Table 3**: Potentially high impact *POR* variants identified in this study. All the variants in this table were initially predicted to be deleterious while using the conventional CADD score threshold >15.15.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **#** | **Core Variants** | **Consequence** | **CADDa** | **CADDb** | **SIFT** | **PolyPhen-2** | **LRT** | **PROVEAN** | **VEST4** |
| 1 | rs375535318 | Missense Variant(R453H) | X | X | X | X | X | X | X |
| 2 | rs375406404 | Missense Variant(V678M) | X | X | X | X | X |  | X |
| 3 | rs369924019 | Missense Variant(V230M) | X | X | X | X | X |  | X |
| 4 | rs569673150 | Missense Variant(G537S) | X | X | X | X | X | X | X |
| 5 | rs72557937 | Missense Variant(P284T) | X | X | X | X | X | X | X |
| 6 | rs72557946 | Missense Variant(V472M) | X | X | X | X | X |  | X |
| 7 | rs374967948 | Missense Variant(A172V) | X | X |  | X | X | X | X |
| 8 | rs374141883 | Missense Variant (R509C) | X | X | X | X | X |  | X |
| 9 | rs200622912 | Missense Variant(H106R) | X | X |  |  | X |  | X |
| 10 | rs377283521 | Missense Variant (M656I) | X | X |  |  | X |  | X |
| 11 | rs72553987 | inframe deletion (KE53K) | X | X |  |  |  |  |  |
| 12 | rs372930296 | Missense Variant(D648N) | X | X |  |  | X |  |  |
| 13 | rs532294040 | Missense Variant(Q201R) | X |  |  |  | X |  |  |
| 14 | rs8509 | downstream variant | X |  |  |  |  |  |  |
| 15 | rs3823884 | upstream variant | X |  |  |  |  |  |  |
| 16 | rs1057868 | Missense Variant(A503V) | X |  |  |  |  |  |  |
| 17 | rs571978393 | Intron variant | X |  |  |  |  |  |  |
| 18 | rs782127423 | Splice donor, Intron variant | X |  |  |  |  |  |  |
| 19 | rs545021910 | Intron variant | X |  |  |  |  |  |  |
| 20 | rs11983044 | Intron variant | X |  |  |  |  |  |  |
| 21 | rs929777906 | Intron variant | X |  |  |  |  |  |  |
| 22 | rs538316500 | Missense Variant (R361W) | X | X | X | X |  | X | X |
| 23 | rs536353066 | Missense Variant (W422G) | X | X | X | X | X | X | X |
| 24 | rs534798705 | Missense Variant (G557V) | X | X | X | X | X | X | X |
| 25 | rs564863959 | Missense Variant (G175S) | X | X |  | X | X | X | X |
| 26 | rs72557914 | Missense Variant (D211N) | X | X | X | X | X | X | X |
| 27 | rs374707345 | Missense Variant (D212N) | X | X | X | X | X | X | X |
| 28 | rs557802016 | Missense Variant (R268Q) | X | X | X | X | X | X | X |
| 29 | rs28931608 | Missense Variant (R457H) | X | X | X | X | X | X | X |
| 30 | rs547249232 | Missense Variant (R202P) | X | X | X | X | X | X | X |
| 31 | rs202243657 | Missense Variant (R406C) | X | X | X | X | X | X | X |
| 32 | rs145028213 | Missense Variant (R517C) | X | X | X | X | X | X | X |
| 33 | rs540924885 | Missense Variant (V323M) | X | X | X | X | X |  | X |
| 34 | rs782247167 | Missense Variant (R571C) | X | X | X | X | X | X | X |
| 35 | rs574381787 | Missense Variant (R487H) | X | X | X | X | X | X | X |
| 36 | rs72557950 | Missense Variant (R600W) | X | X | X | X | X | X | X |
| 37 | rs200097755 | Missense Variant (R301C) | X | X | X | X | X | X | X |
| 38 | rs555871077 | Missense Variant (L308W) | X | X | X | X | X |  | X |
| 39 | rs375378703 | Missense Variant (Y156C) | X | X | X | X | X | X | X |
| 40 | rs1554558754 | Missense Variant (C366G) | X | X | X | X | X | X | X |
| 41 | rs545968903 | Missense Variant (A597V) | X | X | X | X | X | X | X |
| 42 | rs557738416 | Missense Variant (Y43D) | X | X | X | X | X | X | X |
| 43 | rs72557935 | Missense Variant (P542L) | X | X | X | X | X | X | X |
| 44 | rs17853284 | Missense Variant (P228L) | X | X | X | X | X | X | X |
| 45 | rs539404456 | Missense Variant (A635V) | X | X | X | X | X | X | X |
| 46 | rs72557936 | Missense Variant (A462T) | X | X | X |  | X |  | X |
| 47 | rs11540674 | Missense Variant (E300K) | X | X | X |  | X |  | X |
| 48 | rs565343242 | Missense Variant (G507S) | X | X |  | X | X |  | X |
| 49 | rs562241770 | Missense Variant (V334I) | X | X | X | X | X |  | X |
| 50 | rs574694698 | Missense Variant (T563M) | X | X |  | X | X | X | X |
| 51 | rs575786687 | Missense Variant (N382D) | X | X |  |  | X |  | X |
| 52 | rs201960141 | Missense Variant (G338A) | X | X |  | X | X | X | X |
| 53 | rs200249978 | Missense Variant (S397L) | X | X | X | X |  | X | X |
| 54 | rs554641893 | Missense Variant (R441Q) | X | X |  |  | X |  | X |
| 55 | rs190570042 | Missense Variant (T375A) | X | X |  |  | X |  | X |
| 56 | rs543360508 | Missense Variant (P384L) | X | X |  | X | X | X | X |
| 57 | rs148175064 | Missense Variant (V650M) | X | X | X |  | X |  |  |
| 58 | rs41299514 | Missense Variant (D255N) | X | X | X |  | X | X | X |
| 59 | rs199634961 | Missense Variant (A115V) | X | X |  |  | X | X | X |
| 60 | rs567904247 | Missense Variant (G413S) | X | X |  |  |  |  |  |
| 61 | rs782343229 | Missense Variant (A527V) | X | X |  |  | X |  |  |
| 62 | - | Missense Variant (V261L) | X | X |  |  | X |  | X |
| 63 | - | Missense Variant (P443A) | X | X |  |  | X |  | X |
| 64 | rs376509000 | Missense Variant (R571H) | X | X |  |  | X |  |  |
| 65 | rs377159530 | Missense Variant (E505K) | X | X |  |  | X |  | X |
| 66 | rs72553987 | Inframe deletion (KE51Kfs) | X | X |  |  |  |  |  |
| 67 | rs782697310 | Missense Variant (E501K) | X | X |  |  |  |  |  |
| 68 | rs557324700 | Missense Variant (V251M) | X | X |  |  | X |  |  |
| 69 | rs372930296 | Missense Variant (D624N) | X | X |  |  | X |  |  |
| 70 | rs72557946 | Missense Variant (V472L) | X | X | X | X | X |  | X |
| 71 | rs566582879 | Missense Variant (I60V) | X | X |  |  | X |  |  |
| 72 | rs150949148 | Missense Variant (A172T) | X | X |  |  | X |  |  |
| 73 | rs374350596 | Missense Variant (S35L) | X |  |  |  | X | X | X |
| 74 | rs370645073 | Missense Variant (S572L) | X |  |  |  |  |  |  |
| 75 | rs145782750 | Missense Variant (V631I) | X |  |  |  | X |  | X |
| 76 | rs558340290 | Missense Variant (P649A) | X |  |  |  | X | X |  |

The presence of an ‘X’ indicates a deleterious outcome for the variant as predicted by the *in silico* tool. CADDa is the prediction before implementing ADME-optimised parameters. CADDb is the prediction after implementing ADME-optimised parameters. The ADME-optimised deleteriousness thresholds are as follows: CADD > 19.19; SIFT < 0.0376; Polyphen-2 > 0.3841; LRT < 0.0025; PROVEAN < -3.286; VEST4 > 0.4534. Variants 1-21 were present in the sub-Saharan African populations in this study while the rest were only found in the other global populations from the 1000 Genomes Project Dataset.

**Plug-in scores corresponding to variants listed above**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| # | **Core variant** | **Consequence** | **SIFT** | **PolyPhen-2** | **LRT** | **PROVEAN** | **VEST4** | **CADD** |
| 1 | rs375535318 | Missense Variant(R453H) | 0 | 0.999 | 0.000001 | -4.9 | 0.743 | 29 |
| 2 | rs375406404 | Missense Variant(V678M) | 0 | 0.998 | 0.00024 | -2.81 | 0.742 | 27.3 |
| 3 | rs369924019 | Missense Variant(V230M) | 0.01 | 0.542 | 0.000004 | -2.56 | 0.803 | 26.6 |
| 4 | rs569673150 | Missense Variant(G537S) | 0 | 1 | 0 | -5.56 | 0.975 | 26 |
| 5 | rs72557937 | Missense Variant(P284T) | 0 | 1 | 0 | -7.79 | 0.843 | 25.4 |
| 6 | rs72557946 | Missense Variant(V472M) | 0 | 0.953 | 0.000002 | -2.45 | 0.507 | 24.5 |
| 7 | rs374967948 | Missense Variant(A172V) | 0.07 | 0.396 | 0 | -3.52 | 0.709 | 23.4 |
| 8 | rs374141883 | Missense Variant (R509C) | 0.02 | 0.676 | 0.000838 | -3.14 | 0.56403 | 24.2 |
| 9 | rs200622912 | Missense Variant(H106R) | 0.57 | 0.009 | 0 | -2.06 | 0.542 | 21.9 |
| 10 | rs377283521 | Missense Variant (M656I) | 0.06 | 0.011 | 0.000019 | -3.01 | 0.05929 | 21.6 |
| 11 | rs72553987 | inframe deletion (KE53K) | - | - | - | - | - | 21.3 |
| 12 | rs372930296 | Missense Variant(D648N) | 0.11 | 0 | 0.000512 | -1.01 | 0.157 | 20.2 |
| 13 | rs532294040 | Missense Variant(Q201R) | 0.57 | 0.001 | 0.000268 | -0.85 | 0.332 | 18.95 |
| 14 | rs8509 | Downstream Variant | - | - | - | - | - | 17.86 |
| 15 | rs3823884 | Upstream variant | - | - | - | - | - | 17.42 |
| 16 | rs1057868 | Missense Variant(A503V) | 0.35 | 0 | 0.002907 | -0.7 | 0.089 | 15.15 |
| 17 | rs571978393 | Intron variant | - | - | - | - | - | 15.08 |
| 18 | rs782127423 | Splice donor, Intron variant | - | - | - | - | - | 17.27 |
| 19 | rs545021910 | Intron variant |  |  |  |  |  | 17.08 |
| 20 | rs11983044 | Intron variant | - | - | - | - | - | 15.56 |
| 21 | rs929777906 | Intron variant | - | - | - | - | - | 15.41 |
| 22 | rs538316500 | Missense Variant (R361W) | 0 | 0.989 | 0.311079 | -7.33 | 0.9775 | 33 |
| 23 | rs536353066 | Missense Variant (W422G) | 0.01 | 0.971 | 0.000006 | -12.26 | 0.91391 | 33 |
| 24 | rs534798705 | Missense Variant (G557V) | 0 | 0.81 | 0.000006 | -7.46 | 0.89242 | 33 |
| 25 | rs564863959 | Missense Variant (G175S) | 0.04 | 0.871 | 0.000005 | -5.01 | 0.62273 | 32 |
| 26 | rs72557914 | Missense Variant (D211N) | 0 | 0.999 | 0 | -4.8 | 0.75009 | 32 |
| 27 | rs374707345 | Missense Variant (D212N) | 0 | 1 | 0 | -4.62 | 0.73735 | 32 |
| 28 | rs557802016 | Missense Variant (R268Q) | 0.01 | 0.911 | 0.000001 | -3.87 | 0.82157 | 32 |
| 29 | rs28931608 | Missense Variant (R457H) | 0 | 1 | 0 | -4.97 | 0.9884 | 32 |
| 30 | rs547249232 | Missense Variant (R202P) | 0.01 | 1 | 0 | -6.55 | 0.95725 | 31 |
| 31 | rs202243657 | Missense Variant (R406C) | 0.01 | 0.732 | 0 | -4.58 | 0.78262 | 31 |
| 32 | rs145028213 | Missense Variant (R517C) | 0 | 0.999 | 0 | -7.58 | 0.91047 | 29.8 |
| 33 | rs540924885 | Missense Variant (V323M) | 0.02 | 0.819 | 0 | -1.66 | 0.94314 | 29 |
| 34 | rs782247167 | Missense Variant (R571C) | 0.01 | 0.891 | 0.000002 | -4.57 | 0.52208 | 28.8 |
| 35 | rs574381787 | Missense Variant (R487H) | 0.02 | 0.995 | 0 | -4.52 | 0.85766 | 28.2 |
| 36 | rs72557950 | Missense Variant (R600W) | 0 | 0.998 | 0 | -7.58 | 0.90138 | 27.9 |
| 37 | rs200097755 | Missense Variant (R301C) | 0 | 0.997 | 0.000002 | -7.17 | 0.95256 | 27.3 |
| 38 | rs555871077 | Missense Variant (L308W) | 0 | 0.994 | 0.000022 | -2.54 | 0.93487 | 27.3 |
| 39 | rs375378703 | Missense Variant (Y156C) | 0 | 0.992 | 0.000001 | -7.82 | 0.84817 | 27.1 |
| 40 | rs1554558754 | Missense Variant (C366G) | 0 | 0.906 | 0 | -11.58 | 0.86404 | 26.8 |
| 41 | rs545968903 | Missense Variant (A597V) | 0 | 1 | 0.000001 | -3.79 | 0.88909 | 26.6 |
| 42 | rs557738416 | Missense Variant (Y43D) | 0.01 | 0.905 | 0.000058 | -10 | 0.83576 | 26.4 |
| 43 | rs72557935 | Missense Variant (P542L) | 0 | 0.999 | 0 | -9.64 | 0.95256 | 26.3 |
| 44 | rs17853284 | Missense Variant (P228L) | 0 | 0.584 | 0 | -8.57 | 0.88137 | 26 |
| 45 | rs539404456 | Missense Variant (A635V) | 0.01 | 0.999 | 0 | -3.78 | 0.84194 | 25.2 |
| 46 | rs72557936 | Missense Variant (A462T) | 0 | 0.109 | 0 | -1.46 | 0.9455 | 25 |
| 47 | rs11540674 | Missense Variant (E300K) | 0.02 | 0.015 | 0.000979 | -2.64 | 0.59393 | 24.6 |
| 48 | rs565343242 | Missense Variant (G507S) | 0.05 | 0.863 | 0 | -1.74 | 0.61256 | 24.5 |
| 49 | rs562241770 | Missense Variant (V334I) | 0.03 | 0.581 | 0 | -0.88 | 0.92433 | 24.4 |
| 50 | rs574694698 | Missense Variant (T563M) | 0.17 | 0.911 | 0 | -4.25 | 0.76203 | 24.4 |
| 51 | rs575786687 | Missense Variant (N382D) | 0.04 | 0.136 | 0.000001 | -1.72 | 0.64648 | 23.5 |
| 52 | rs201960141 | Missense Variant (G338A) | 0.25 | 0.572 | 0.000003 | -5.13 | 0.64393 | 23.2 |
| 53 | rs200249978 | Missense Variant (S397L) | 0.02 | 0.39 | 0.047508 | -4.27 | 0.49874 | 23.2 |
| 54 | rs554641893 | Missense Variant (R441Q) | 0.12 | 0.077 | 0.000001 | -1.86 | 0.46928 | 23.1 |
| 55 | rs190570042 | Missense Variant (T375A) | 0.05 | 0.036 | 0 | -3.15 | 0.76388 | 23 |
| 56 | rs543360508 | Missense Variant (P384L) | 0.07 | 0.914 | 0 | -8.78 | 0.9875 | 23 |
| 57 | rs148175064 | Missense Variant (V650M) | 0.02 | 0.383 | 0.000214 | -1.41 | 0.44474 | 23 |
| 58 | rs41299514 | Missense Variant (D255N) | 0.02 | 0.066 | 0 | -4.04 | 0.61849 | 22.9 |
| 59 | rs199634961 | Missense Variant (A115V) | 0.21 | 0.328 | 0 | -3.33 | 0.97961 | 22.8 |
| 60 | rs567904247 | Missense Variant (G413S) | 0.51 | 0.01 | 0.00576 | 0.01 | 0.40864 | 22.7 |
| 61 | rs782343229 | Missense Variant (A527V) | 0.33 | 0 | 0.000776 | -1.24 | 0.34552 | 22.7 |
| 62 | - | Missense Variant (V261L) | 0.34 | 0.007 | 0.000016 | -1.62 | 0.70527 | 22 |
| 63 | - | Missense Variant (P443A) | 0.09 | 0.179 | 0 | -5.22 | 0.80375 | 21.8 |
| 64 | rs376509000 | Missense Variant (R571H) | 0.74 | 0.003 | 0.000002 | -0.44 | 0.16586 | 21.7 |
| 65 | rs377159530 | Missense Variant (E505K) | 0.39 | 0.045 | 0.000064 | -1.44 | 0.54059 | 21.5 |
| 66 | rs72553987 | Inframe deletion (KE51Kfs) | - | - | - | - | - | 21.3 |
| 67 | rs782697310 | Missense Variant (E501K) | 0.9 | 0 | 0.044091 | -0.02 | 0.38438 | 20.4 |
| 68 | rs557324700 | Missense Variant (V251M) | 0.12 | 0.007 | 0.000475 | -1 | 0.40465 | 20.2 |
| 69 | rs372930296 | Missense Variant (D624N) | 0.11 | 0 | 0.000512 | -1.01 | 0.16308 | 20.2 |
| 70 | rs72557946 | Missense Variant (V472L) | 0.1 | 0.062 | 0.000002 | -1.91 | 0.55019 | 19.67 |
| 71 | rs566582879 | Missense Variant (I60V) | 0.2 | 0.011 | 0.00048 | -0.83 | 0.25867 | 19.56 |
| 72 | rs150949148 | Missense Variant (A172T) | 0.13 | 0.029 | 0 | -3.01 | 0.34659 | 19.46 |
| 73 | rs374350596 | Missense Variant (S35L) | 0.42 | 0.005 | 0.002131 | -5.89 | 0.76296 | 19.06 |
| 74 | rs370645073 | Missense Variant (S572L) | 0.06 | 0.138 | 0.014346 | -2.69 | 0.14905 | 19.03 |
| 75 | rs145782750 | Missense Variant (V631I) | 0.45 | 0.014 | 0.000096 | -0.39 | 0.69913 | 17.56 |
| 76 | rs558340290 | Missense Variant (P649A) | 0.06 | 0.006 | 0 | -6.81 | 0.3895 | 15.34 |