Regulatory polymorphisms in *CYP2C19* affecting hepatic expression
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**Supplemental Table 3:** Ion Torrent Sequencing SNP calls
(A) SNPs called with minimum 20 reads and 30% allele frequency. Color coded legend indicates comparisons between L114 (AEI-) and LL16, LL19 (AEI+)
Reference Sequence: NG_008384

Likely Artifact- Indicated by generally lower coverage compared to other areas of the genome. Also non unique to AEI+ subjects

| |
|---|
| Unique Regulatory Region SNP |
| Present in AEI- negative |
| Potentially part of *CYP2C19*20(CYP2C19*3B)* haplotype, however L123 did not contain the functional SNP (rs4986893) |
| Unique to AEI postive samples but not consistently present in other *17 carriers namely LL48 (*17/*17) and LL44 (VMAX outlier) |
| In high LD with rs12248560 r2=1, D`=1 in CEU (1K Genomes)<br>No indication in change of splicing in humans (http://regrna.mbc.nctu.edu.tw/html/prediction.html)<br>or polyA (http://www.imtech.res.in/raghava/polyapred/submission.html) |

| **L114** | AEI- | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| rs# | Reference Position | Variation Type | Reference | Variants | Allele Vari | Frequencies | Counts | Coverage |
| rs74152364 | 1243 | SNP | C | 2 | T/C | 53.7/46.2 | 378/325 | 704 |
| rs78721914 | 1382 | SNP | A | 2 | A/G | 58.6/41.4 | 284/201 | 485 |
| rs78742448 | 1670 | SNP | C | 2 | C/T | 60.1/39.1 | 309/201 | 514 |
| rs78535200 | 1672 | SNP | G | 2 | G/T | 57.7/41.6 | 297/214 | 515 |
| rs4532967 | 1735 | SNP | G | 2 | T/G | 51.1/48.6 | 334/318 | 654 |
| rs77046614 | 1782 | SNP | T | 2 | T/G | 51.7/48.2 | 344/321 | 666 |
| rs77957608 | 2229 | SNP | G | 2 | G/A | 57.3/42.7 | 519/387 | 906 |
| rs77850210 | 2281 | SNP | T | 2 | C/T | 58.0/41.9 | 568/411 | 980 |
| rs3814637 | 3583 | SNP | C | 2 | C/T | 51.7/47.7 | 169/156 | 327 |
| rs11568732 | 4112 | SNP | T | 2 | G/T | 50.0/49.8 | 230/229 | 460 |
| no rs# | 4334 | SNP | A | 2 | A/T | 68.9/31.1 | 93/42 | 135 |
| rs4986894 | 4903 | SNP | T | 2 | T/C | 50.8/48.9 | 190/183 | 374 |
| rs17885098 | 5099 | SNP | C | 2 | T/C | 60.8/38.4 | 371/234 | 610 |
| rs17884832 | 17013 | SNP | T | 2 | T/G | 58.8/40.8 | 144/100 | 245 |
| rs7916649 | 17122 | SNP | G | 1 | A | 100 | 267 | 267 |
| rs17878459 | 17460 | SNP | G | 2 | C/G | 51.9/48.1 | 94/87 | 181 |
| rs12769205 | 17662 | SNP | A | 2 | G/A | 50.0/48.4 | 92/89 | 184 |
| rs17879992 | 18166 | SNP | T | 2 | T/C | 61.3/38.7 | 119/75 | 194 |
| no rs# | 84698 | SNP | T | 2 | T/A | 65.0/30.0 | 13/6 | 20 |
| rs28399513 | 84936 | SNP | T | 2 | T/A | 55.7/43.6 | 83/65 | 149 |
| rs3758580 | 85160 | SNP | C | 2 | C/T | 52.0/47.1 | 115/104 | 221 |
| rs3758581 | 85161 | SNP | A | 2 | A/G | 51.8/48.2 | 114/106 | 220 |
| rs17885052 | 92620 | SNP | A | 2 | A/T | 55.8/43.7 | 226/177 | 405 |
| no rs# | 92745 | SNP | G | 2 | G/T | 68.6/31.4 | 131/60 | 191 |

| **LL16** | AEI+ | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| rs# | Reference Position | Variation Type | Reference | Variants | Allele Vari | Frequencies | Counts | Coverage |
| rs74152364 | 1243 | SNP | C | 2 | T/C | 55.3/44.4 | 264/212 | 477 |
| rs78721914 | 1382 | SNP | A | 2 | A/G | 50.6/48.8 | 173/167 | 342 |
| rs11188072 | 1599 | SNP | C | 2 | T/C | 53.4/46.6 | 254/222 | 476 |
| rs78742448 | 1670 | SNP | C | 2 | T/C | 51.1/48.3 | 250/236 | 489 |
| rs78535200 | 1672 | SNP | G | 2 | G/T | 50.0/48.9 | 232/227 | 464 |
| rs77046614 | 1782 | SNP | T | 2 | G/T | 54.0/45.7 | 339/287 | 628 |
| rs77957608 | 2229 | SNP | G | 2 | G/A | 51.8/48.2 | 393/365 | 758 |
| rs77850210 | 2281 | SNP | T | 2 | C/T | 60.0/39.9 | 512/341 | 854 |
| rs3814637 | 3583 | SNP | C | 2 | T/C | 51.9/48.0 | 407/376 | 784 |
| rs11568732 | 4112 | SNP | T | 2 | T/G | 51.3/48.6 | 520/493 | 1014 |
| rs12248560 | 4195 | SNP | C | 2 | C/T | 51.9/48.1 | 694/644 | 1338 |
| rs17885098 | 5099 | SNP | C | 2 | T/C | 59.7/39.1 | 863/566 | 1446 |
| rs17884832 | 17013 | SNP | T | 2 | T/G | 55.8/44.1 | 449/355 | 805 |
| rs7916649 | 17122 | SNP | G | 1 | A | 99.8 | 889 | 891 |
| rs17879992 | 18166 | SNP | T | 2 | T/C | 55.5/44.5 | 267/214 | 481 |
| rs4304697 | 23427 | SNP | G | 2 | A/G | 63.0/36.6 | 153/89 | 243 |
| rs7088784 | 23911 | SNP | A | 2 | A/G | 62.1/37.0 | 131/78 | 211 |
| rs55732648 | 62602 | SNP | A | 2 | T/A | 52.5/47.3 | 3371/3038 | 6419 |
| rs28399511 | 62678 | SNP | T | 2 | G/T | 51.4/48.4 | 3434/3231 | 6680 |
| rs3758581 | 85161 | SNP | A | 2 | G/A | 56.8/43.2 | 336/256 | 592 |
| rs17885052 | 92620 | SNP | A | 2 | A/T | 57.4/42.6 | 179/133 | 312 |
| no rs# | 92745 | SNP | G | 2 | G/T | 64.5/35.5 | 80/44 | 124 |
| rs12268020 | 94909 | SNP | C | 2 | C/T | 53.8/46.2 | 56/48 | 104 |

| **LL19** | AEI+ | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| rs# | Reference Position | Variation Type | Reference | Variants | Allele Vari | Frequencies | Counts | Coverage |
| rs74152364 | 1243 | SNP | C | 2 | T/C | 53.3/46.4 | 517/450 | 970 |
| rs78721914 | 1382 | SNP | A | 2 | A/G | 53.8/45.6 | 364/309 | 677 |
| rs11188072 | 1599 | SNP | C | 2 | T/C | 50.7/49.3 | 356/346 | 702 |
| rs78742448 | 1670 | SNP | C | 2 | C/T | 50.5/49.2 | 316/308 | 626 |
| rs78535200 | 1672 | SNP | G | 2 | G/T | 49.3/49.3 | 303/303 | 614 |
| rs77046614 | 1782 | SNP | T | 2 | G/T | 51.1/48.8 | 418/399 | 818 |
| rs77957608 | 2229 | SNP | G | 2 | G/A | 57.4/42.6 | 1354/1005 | 2359 |
| rs77850210 | 2281 | SNP | T | 2 | C/T | 58.0/41.7 | 1551/1116 | 2674 |
| rs3814637 | 3583 | SNP | C | 2 | C/T | 55.7/44.1 | 642/508 | 1152 |
| rs11568732 | 4112 | SNP | T | 2 | T/G | 54.9/45.0 | 766/628 | 1396 |
| rs12248560 | 4195 | SNP | C | 2 | T/C | 53.6/46.4 | 1085/941 | 2026 |
| no rs# | 4334 | SNP | A | 2 | A/T | 67.5/32.3 | 388/186 | 575 |
| rs17885098 | 5099 | SNP | C | 2 | T/C | 61.8/37.0 | 1123/672 | 1817 |
| rs17884832 | 17013 | SNP | T | 2 | T/G | 55.0/45.0 | 403/330 | 733 |
| rs7916649 | 17122 | SNP | G | 1 | A | 99.4 | 821 | 826 |
| rs17879992 | 18166 | SNP | T | 2 | T/C | 54.2/45.8 | 313/265 | 578 |
| rs55732648 | 62602 | SNP | A | 2 | T/A | 52.5/47.3 | 2326/2096 | 4429 |
| rs28399511 | 62678 | SNP | T | 2 | G/T | 51.4/48.4 | 2426/2281 | 4717 |
| rs3758581 | 85161 | SNP | A | 2 | G/A | 53.1/46.6 | 554/487 | 1044 |
| rs17885052 | 92620 | SNP | A | 2 | A/T | 54.1/45.7 | 218/184 | 403 |
| rs12268020 | 94909 | SNP | C | 2 | T/C | 51.6/48.4 | 49/46 | 95 |

| **L123** | AEI+ | African American | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Reference Position | Variation Type | Reference | Variants | Allele Vari | Frequencies | Counts | Coverage |
| rs7919698 | 497 | SNP | A | 2 | G/A | 63.6/36.4 | 21/12 | 33 |
| rs74152364 | 1243 | SNP | C | 2 | C/T | 55.8/44.2 | 24/19 | 43 |
| rs78721914 | 1382 | SNP | A | 2 | A/G | 61.8/38.2 | 63/39 | 102 |
| rs7101258 | 1669 | SNP | A | 2 | A/C | 56.2/43.8 | 36/28 | 64 |
| rs3814637 | 3583 | SNP | C | 2 | C/T | 56.3/43.7 | 49/38 | 87 |
| rs11568730 | 3610 | SNP | T | 2 | T/G | 53.9/46.1 | 41/35 | 76 |
| rs11568732 | 4112 | SNP | T | 2 | T/G | 62.7/37.3 | 74/44 | 118 |
| rs17885098 | 5099 | SNP | C | 2 | T/C | 51.8/48.2 | 43/40 | 83 |
| rs7916649 | 17122 | SNP | G | 2 | A/G | 63.5/36.5 | 33/19 | 52 |
| rs17878649 | 17306 | SNP | G | 2 | A/G | 51.4/48.6 | 37/35 | 72 |
| rs17879992 | 18166 | SNP | T | 2 | C/T | 58.3/41.7 | 81/58 | 139 |
| rs4304697 | 23427 | SNP | G | 1 | A | 73.2 | 30 | 41 |
| rs7088784 | 23911 | SNP | A | 2 | A/G | 63.8/36.2 | 37/21 | 58 |
| rs56043006 | 62638 | SNP | C | 2 | A/C | 53.8/46.2 | 78/67 | 145 |

**(B)** LL44 and LL48 SNP calling used the same constraints as Supplemental Table 3A.
Additional control samples SNPs were called with minimum of 10 reads and 20 % per allele
Colored legend indicates comparison between outlier LL44 and control samples,
including haplotype information from http://www.cypalleles.ki.se/cyp2c19.htm

Reference Sequence: NG_008384

Known SNP in *2 Haplotypes
Present in control Vmax subjects
Likely heterozygote, heterozygosity confirmed by SNAPSHoT

| **LL44** | *2/*17 Outlier | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Reference Position | Variation Type | Reference | Variants | Allele Vari | Frequencies | Counts | Coverage |
| rs11188072 | 1599 | SNP | C | 2 | T/C | 51.9/48.1 | 208/193 | 401 |
| rs4532967 | 1735 | SNP | G | 2 | T/G | 52.2/47.5 | 211/192 | 404 |
| rs12248560 | 4195 | SNP | C | 2 | C/T | 62.1/37.9 | 36/22 | 58 |
| rs4986894 | 4903 | SNP | T | 1 | C | 76.8 | 43 | 56 |
| rs17885098 | 5099 | SNP | C | 1 | T | 98.2 | 54 | 55 |
| rs7916649 | 17122 | SNP | G | 1 | A | 99.8 | 409 | 410 |
| rs17878459 | 17460 | SNP | G | 2 | G/C | 53.5/46.1 | 130/112 | 243 |
| rs12769205 | 17662 | SNP | A | 2 | A/G | 57.7/41.4 | 138/99 | 239 |
| rs4244285 | 24154 | SNP | G | 2 | A/G | 57.6/42.4 | 178/131 | 309 |
| rs12571421 | 24520 | SNP | A | 2 | G/A | 55.3/44.7 | 378/305 | 683 |
| rs4417205 | 62740 | SNP | C | 2 | G/C | 50.0/49.9 | 1223/1219 | 2444 |
| rs28399513 | 84936 | SNP | T | 2 | T/A | 51.4/48.6 | 112/106 | 218 |
| rs3758580 | 85160 | SNP | C | 2 | T/C | 51.1/48.9 | 158/151 | 309 |
| rs3758581 | 85161 | SNP | A | 1 | G | 98.7 | 306 | 310 |
| rs12268020 | 94909 | SNP | C | 2 | T/C | 54.9/45.1 | 157/129 | 286 |

| **LL1** | *2/*17 | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Reference Position | Variation Type | Reference | Variants | Allele Vari | Frequencies | Counts | Coverage |
| rs11188072 | 1599 | SNP | C | 2 | T/C | 60.0/40.0 | 9_6 | 15 |
| rs4532967 | 1735 | SNP | G | 2 | G/T | 52.6/47.4 | 10_9 | 19 |
| rs12248560 | 4195 | SNP | C | 2 | C/T | 56.0/44.0 | 65/51 | 116 |
| rs4986894 | 4903 | SNP | T | 2 | T/C | 52.5/45.5 | 53/46 | 101 |
| rs17885098 | 5099 | SNP | C | 1 | T | 99 | 102 | 103 |
| rs7916649 | 17122 | SNP | G | 1 | A | 100 | 30 | 30 |
| rs12769205 | 17662 | SNP | A | 2 | A/G | 60.0/40.0 | 12_8 | 20 |
| rs4244285 | 24154 | SNP | G | 2 | A/G | 50.0/50.0 | 13/13 | 26 |
| rs12571421 | 24520 | SNP | A | 2 | A/G | 58.0/42.0 | 51/37 | 88 |
| no rs# | 62664 | SNP | T | 2 | T/A | 62.5/37.5 | 10_6 | 16 |
| rs4417205 | 62740 | SNP | C | 2 | C/G | 51.9/48.1 | 27/25 | 52 |
| rs28399513 | 84936 | SNP | T | 2 | T/A | 54.1/45.9 | 20/17 | 37 |
| rs3758580 | 85160 | SNP | C | 2 | C/T | 65.6/34.4 | 21/11 | 32 |
| rs3758581 | 85161 | SNP | A | 1 | G | 97.1 | 34 | 35 |

| **LL11** | *2/*17 | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Reference Position | Variation Type | Reference | Variants | Allele Vari | Frequencies | Counts | Coverage |
| rs115939780 | 865 | SNP | C | 2 | C/T | 80.0/20.0 | 8_2 | 10 |
| rs12248560 | 4195 | SNP | C | 2 | C/T | 50.9/49.1 | 27/26 | 53 |
| rs4986894 | 4903 | SNP | T | 2 | C/T | 55.6/44.4 | 20/16 | 36 |
| rs17885098 | 5099 | SNP | C | 1 | T | 100 | 45 | 45 |
| rs7916649 | 17122 | SNP | G | 1 | A | 97.1 | 33 | 34 |
| rs17878459 | 17460 | SNP | G | 2 | C/G | 56.8/43.2 | 21/16 | 37 |
| rs12769205 | 17662 | SNP | A | 2 | G/A | 63.0/37.0 | 17/10 | 27 |
| no rs# | 23453 | SNP | G | 2 | G/A | 71.4/28.6 | 15/6 | 21 |
| rs4244285 | 24154 | SNP | G | 2 | A/G | 56.0/44.0 | 14/11 | 25 |
| rs12571421 | 24520 | SNP | A | 2 | A/G | 54.0/46.0 | 27/23 | 50 |
| rs4417205 | 62740 | SNP | C | 2 | C/G | 53.8/46.2 | 28/24 | 52 |

| **LL13** | *2/*17 | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Reference Position | Variation Type | Reference | Variants | Allele Vari | Frequencies | Counts | Coverage |
| rs12248560 | 4195 | SNP | C | 2 | C/T | 51.4/48.6 | 36/34 | 70 |
| rs4986894 | 4903 | SNP | T | 2 | T/C | 53.1/46.9 | 26/23 | 49 |
| rs17885098 | 5099 | SNP | C | 1 | T | 100 | 74 | 74 |
| rs17878459 | 17460 | SNP | G | 2 | G/C | 54.5/36.4 | 6_4 | 11 |
| no rs# | 17981 | SNP | A | 2 | A/G | 80.0/20.0 | 8_2 | 10 |
| rs4244285 | 24154 | SNP | G | 2 | A/G | 50.0/50.0 | 7_7 | 14 |
| rs12571421 | 24520 | SNP | A | 2 | A/G | 63.6/36.4 | 21/12 | 33 |
| rs4417205 | 62740 | SNP | C | 2 | G/C | 58.3/41.7 | 5_7 | 12 |

| **LL45** | *17/*17 | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Reference Position | Variation Type | Reference | Variants | Allele Vari | Frequencies | Counts | Coverage |
| rs11188072 | 1599 | SNP | C | 1 | T | 100 | 11 | 11 |
| rs12248560 | 4195 | SNP | C | 1 | T | 100 | 93 | 93 |
| rs17885098 | 5099 | SNP | C | 1 | T | 94 | 78 | 83 |
| rs7916649 | 17122 | SNP | G | 1 | A | 100 | 31 | 31 |
| No rs# | 62664 | SNP | T | 2 | T/A | 70.8/29.2 | 17/7 | 24 |
| rs3758581 | 85161 | SNP | A | 1 | G | 95.2 | 20 | 21 |
| rs12268020 | 94909 | SNP | C | 1 | T | 100 | 16 | 16 |

| **LL46** | *17/*17 | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Reference Position | Variation Type | Reference | Variants | Allele Vari | Frequencies | Counts | Coverage |
| rs12248560 | 4125 | SNP | T | 2 | T/C | 76.9/23.1 | 10_3 | 13 |
| rs17885098 | 4195 | SNP | C | 1 | T | 100 | 39 | 39 |
| rs17885098 | 5099 | SNP | C | 1 | T | 98.1 | 52 | 53 |
| no rs# | 18133 | SNP | T | 2 | T/C | 70.0/30.0 | 7_3 | 10 |
| no rs# | 62664 | SNP | T | 2 | T/A | 70.0/30.0 | 7_3 | 10 |
| rs3758581 | 85161 | SNP | A | 1 | G | 100 | 11 | 11 |

| **LL47** | *1/*2 | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Reference Position | Variation Type | Reference | Variants | Allele Vari | Frequencies | Counts | Coverage |
| #N/A | 1343 | SNP | G | 2 | G/A | 80.0/20.0 | 8_2 | 10 |
| rs4532967 | 1735 | SNP | G | 2 | G/T | 73.7/26.3 | 14/5 | 19 |
| rs4986894 | 4903 | SNP | T | 2 | T/C | 52.9/47.1 | 64/57 | 121 |
| rs17885098 | 5099 | SNP | C | 1 | T | 95.5 | 127 | 133 |
| rs7916649 | 17122 | SNP | G | 2 | G/A | 65.2/34.8 | 30/16 | 46 |
| no rs# | 17358 | SNP | A | 2 | A/C | 65.0/25.0 | 13/5 | 20 |
| rs17878459 | 17460 | SNP | G | 2 | C/G | 57.8/42.2 | 26/19 | 45 |
| rs12769205 | 17662 | SNP | A | 2 | A/G | 57.8/42.2 | 26/19 | 45 |
| rs4244285 | 24154 | SNP | G | 2 | G/A | 60.7/39.3 | 17/11 | 28 |
| rs12571421 | 24520 | SNP | A | 2 | A/G | 57.7/42.3 | 71/52 | 123 |
| rs113833279 | 60084 | SNP | G | 2 | G/A | 72.7/27.3 | 8_3 | 11 |
| no rs# | 62664 | SNP | T | 2 | T/A | 71.0/29.0 | 22/9 | 31 |
| rs4417205 | 62740 | SNP | C | 2 | C/G | 55.8/44.2 | 58/46 | 104 |
| rs28399513 | 84936 | SNP | T | 2 | T/A | 55.6/44.4 | 20/16 | 36 |
| rs3758580 | 85160 | SNP | C | 2 | C/T | 63.3/36.7 | 19/11 | 30 |
| rs3758581 | 85161 | SNP | A | 1 | G | 96.6 | 28 | 29 |

| **LL48** | *17/*17 | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| rs11188072 | 1599 | SNP | C | 1 | T | 99.8 | 461 | 462 |
| rs12248560 | 4195 | SNP | C | 1 | T | 99.5 | 378 | 380 |
| rs17885098 | 5099 | SNP | C | 1 | T | 98.3 | 529 | 538 |
| rs7916649 | 17122 | SNP | G | 1 | A | 99.8 | 886 | 888 |
| rs3758581 | 85161 | SNP | A | 1 | G | 99 | 670 | 677 |
| rs12268020 | 94909 | SNP | C | 1 | T | 94.6 | 123 | 130 |

| **LL49** | *17/*17 | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Reference Position | Variation Type | Reference | Variants | Allele Vari | Frequencies | Counts | Coverage |
| rs11188072 | 1599 | SNP | C | 1 | T | 100 | 40 | 40 |
| rs12248560 | 4195 | SNP | C | 1 | T | 99.2 | 260 | 262 |
| rs17885098 | 5099 | SNP | C | 1 | T | 96.9 | 246 | 254 |
| rs7916649 | 17122 | SNP | G | 1 | A | 98.8 | 84 | 85 |
| rs3758581 | 22098 | SNP | A | 2 | A/G | 72.7/27.3 | 8_3 | 11 |
| no rs# | 84611 | SNP | T | 2 | T/C | 61.5/38.5 | 8_5 | 13 |
| rs3758581 | 85161 | SNP | A | 1 | G | 100 | 68 | 68 |
| rs12268020 | 94909 | SNP | C | 1 | T | 87.9 | 29 | 33 |

| **LL53** | *17/*17 | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Reference Position | Variation Type | Reference | Variants | Allele Vari | Frequencies | Counts | Coverage |
| rs12248560 | 4195 | SNP | C | 1 | T | 98.8 | 158 | 160 |
| rs17885098 | 5099 | SNP | C | 1 | T | 94.2 | 131 | 139 |
| rs7916649 | 17122 | SNP | G | 1 | A | 100 | 31 | 31 |
| rs3758581 | 85161 | SNP | A | 1 | G | 100 | 22 | 22 |