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**eFigure 5.** Associations of each SNP genotype with DNA methylation at 221 arsenic-associated CpGs discovered in meta-analysis.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **eTable 1.** CpG sites discovered in HEALS with the EPIC array. | | | | | | | |
| Name | Chromosome | Position | CpG Location | UCSC Gene Name | UCSC Relation to Gene | Direction of Effect | P |
| cg01912040 | 17 | 1106553 | Shore |  |  | ↓ | 4.2 x 10-13 |
| cg05962511 | 10 | 102730022 | Shore |  |  | ↓ | 2.8 x 10-12 |
| cg10003262 | 17 | 1106589 | Shore |  |  | ↓ | 2.5 x 10-11 |
| cg17420142 | 18 | 32702783 |  | MAPRE2 | Body | ↓ | 3.1 x 10-10 |
| cg06466147 | 1 | 155188982 |  | GBAP1 | Body | ↓ | 6.2 x 10-9 |
| cg09082427 | 9 | 140349184 | Shore | NSMF | Body | ↓ | 9.9 x 10-9 |
| cg04193083 | 17 | 41323562 | Shore | NBR1 | 5'UTR | ↑ | 3.3 x 10-8 |
| cg19534475 | 3 | 141632139 |  | ATP1B3 | Body | ↑ | 9.6 x 10-8 |
| cg12608784 | 9 | 140349197 | Shore | NSMF | Body | ↓ | 1.2 x 10-7 |
| cg14891900 | 17 | 76341204 | Shelf |  |  | ↑ | 1.3 x 10-7 |
| cg11308227 | 17 | 79202435 |  | ENTHD2 | 3'UTR | ↓ | 1.3 x 10-7 |
| cg13832772 | 4 | 186283800 |  | SNX25 | Body | ↓ | 1.7 x 10-7 |
| cg15108641 | 10 | 99263320 | Shelf | UBTD1 | Body | ↑ | 2.5 x 10-7 |
| cg09658504 | 9 | 140349188 | Shore | NSMF | Body | ↓ | 3.0 x 10-7 |
| cg05438461 | 15 | 40401720 | Shore | BMF | TSS1500 | ↑ | 3.5 x 10-7 |
| cg10663081 | 20 | 36837543 |  |  |  | ↓ | 3.7 x 10-7 |
| cg08759026 | 11 | 69061454 |  | MYEOV | TSS200 | ↓ | 6.7 x 10-7 |
| cg11644394 | 7 | 144148615 |  |  |  | ↑ | 7.5 x 10-7 |
| cg05428706 | 10 | 102730130 | Shore |  |  | ↓ | 8.2 x 10-7 |
| cg12865207 | 3 | 138669373 | Shore | FOXL2NB | Body | ↑ | 1.0 x 10-6 |
| cg09183146 | 16 | 1429863 | Island | UNKL | TSS200 | ↓ | 1.2 x 10-6 |
| cg04622454 | 9 | 140349128 | Shore | NELF | Body | ↓ | 1.3 x 10-6 |
| cg06381803 | 19 | 46119475 | Island | EML2 | Body | ↓ | 1.4 x 10-6 |
| cg02772605 | 1 | 28912323 | Shelf |  |  | ↑ | 1.4 x 10-6 |
| cg10283165 | 19 | 17375666 |  | USHBP1 | TSS200 | ↓ | 1.4 x 10-6 |
| cg04891961 | 17 | 27939900 | Island | ANKRD13B | Body | ↓ | 1.4 x 10-6 |
| cg12746706 | 6 | 169276508 |  |  |  | ↓ | 1.5 x 10-6 |
| cg02330195 | 10 | 73342047 |  | CDH23 | Body | ↑ | 1.5 x 10-6 |
| cg08077890 | 18 | 157838 | Shore | USP14 | TSS1500 | ↑ | 1.6 x 10-6 |
| cg20433952 | 17 | 55607898 |  | MSI2 | Body | ↓ | 1.9 x 10-6 |
| cg05646745 | 10 | 135172466 | Shore | FUOM | TSS1500 | ↑ | 1.9 x 10-6 |
| cg10185759 | 12 | 60366859 |  |  |  | ↓ | 1.9 x 10-6 |
| cg22345623 | 9 | 125050297 |  | MRRF | Body | ↓ | 2.0 x 10-6 |
| cg13480898 | 19 | 10195914 | Shore | C19orf66 | TSS1500 | ↓ | 2.0 x 10-6 |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **eTable 2.** CpG sites discovered in meta-analysis. | | | | | | | |
| **Name** | **Chromosome** | **Position** | **CpG Location** | **UCSC Gene Name** | **UCSC Relation to Gene** | **Direction of Effect** | **P** |
| cg01912040 | 17 | 1106553 | Shore |  |  | ↓↓ | 3.3 x 10-17 |
| cg10003262 | 17 | 1106589 | Shore |  |  | ↓↓ | 1.9 x 10-15 |
| cg05962511 | 10 | 102730022 | Shore |  |  | ↓↓ | 2.1 x 10-13 |
| cg13480898 | 19 | 10195914 | Shore | C19orf66 | TSS1500 | ↓↓ | 4.1 x 10-13 |
| cg07207669 | 1 | 155102388 | Shore | EFNA1 | Body | ↓↓ | 3.0 x 10-12 |
| cg01225779 | 5 | 179238472 | Shelf | SQSTM1 | 5'UTR | ↓↓ | 1.0 x 10-11 |
| cg06381803 | 19 | 46119475 | Island | EML2 | Body | ↓↓ | 4.8 x 10-11 |
| cg09183146 | 16 | 1429863 | Island | UNKL | TSS200 | ↓↓ | 1.4 x 10-10 |
| cg08759026 | 11 | 69061454 |  | MYEOV | TSS200 | ↓↓ | 2.8 x 10-10 |
| cg17489312 | 1 | 9376039 |  | SPSB1 | 5'UTR | ↓↓ | 2.9 x 10-10 |
| cg00472758 | 16 | 2552820 | Shelf | TBC1D24 | 3'UTR | ↓↓ | 5.6 x 10-10 |
| cg05428706 | 10 | 102730130 | Shore |  |  | ↓↓ | 5.8 x 10-10 |
| cg05425326 | 16 | 58439361 |  | GINS3 | 3'UTR | ↑↑ | 6.1 x 10-10 |
| cg26435149 | 3 | 55605611 |  | ERC2 | 3'UTR | ↓↓ | 7.3 x 10-10 |
| cg17393635 | 19 | 49843565 | Island | CD37 | Body | ↓↓ | 1.2 x 10-9 |
| cg13223043 | 1 | 26492308 | Shore |  |  | ↓↓ | 2.5 x 10-9 |
| cg03871754 | 17 | 79320652 | Island |  |  | ↓↓ | 3.3 x 10-9 |
| cg19240637 | 2 | 7172297 | Island | RNF144A | Body | ↓↓ | 3.7 x 10-9 |
| cg07782285 | 19 | 13085442 |  | DAND5 | 3'UTR | ↓↓ | 7.5 x 10-9 |
| cg26390598 | 21 | 41032396 |  | B3GALT5 | 5'UTR | ↑↑ | 1.0 x 10-8 |
| cg04622454 | 9 | 140349128 | Shore | NELF | Body | ↓↓ | 1.1 x 10-8 |
| cg22959742 | 10 | 13913931 |  | FRMD4A | Body | ↑↑ | 1.3 x 10-8 |
| cg00281776 | 2 | 209224225 | Shore |  |  | ↓↓ | 1.8 x 10-8 |
| cg12261095 | 19 | 7764345 |  | FCER2 | Body | ↓↓ | 2.0 x 10-8 |
| cg14718533 | 10 | 33355576 |  |  |  | ↑↑ | 2.1 x 10-8 |
| cg04459545 | 19 | 17375685 |  | USHBP1 | TSS200 | ↓↓ | 3.1 x 10-8 |
| cg14145338 | 9 | 139649039 |  | LCN8 | Body | ↓↓ | 3.3 x 10-8 |
| cg04920032 | 12 | 50262986 |  | FAIM2 | 3'UTR | ↓↓ | 3.5 x 10-8 |
| cg18413900 | 12 | 58160989 | Shore | CYP27B1 | TSS200 | ↑↑ | 3.6 x 10-8 |
| cg01757312 | 13 | 112720565 | Island | SOX1 | TSS1500 | ↑↑ | 3.7 x 10-8 |
| cg05816193 | 6 | 26018127 | Shelf | HIST1H1A | TSS200 | ↓↓ | 4.4 x 10-8 |
| cg07367302 | 1 | 19967428 | Shelf |  |  | ↓↓ | 4.6 x 10-8 |
| cg02306995 | 3 | 122635049 | Shelf | SEMA5B | Body | ↓↓ | 5.5 x 10-8 |
| cg24318728 | 17 | 39649283 |  |  |  | ↓↓ | 5.9 x 10-8 |
| cg04875062 | 1 | 17305562 | Shore | MFAP2 | 5'UTR | ↓↓ | 6.0 x 10-8 |
| cg13764516 | 9 | 139648911 |  | LCN8 | 3'UTR | ↓↓ | 6.5 x 10-8 |
| cg23050300 | 1 | 3281321 |  | PRDM16 | Body | ↓↓ | 8.4 x 10-8 |
| cg18050715 | 13 | 97996992 | Shore | MBNL2 | Body | ↑↑ | 8.7 x 10-8 |
| cg04826368 | 6 | 27130208 |  |  |  | ↓↓ | 1.0 x 10-7 |
| cg08596618 | 1 | 24275885 |  |  |  | ↓↓ | 1.1 x 10-7 |
| cg27092191 | 16 | 31884699 | Shore | ZNF267 | TSS1500 | ↓↓ | 1.2 x 10-7 |
| cg06378491 | 11 | 64564012 |  | MAP4K2 | Body | ↓↓ | 1.5 x 10-7 |
| cg23233742 | 5 | 139077894 | Shore |  |  | ↓↓ | 1.6 x 10-7 |
| cg04543901 | 17 | 63519783 |  |  |  | ↓↓ | 2.1 x 10-7 |
| cg11921539 | 11 | 116328665 |  |  |  | ↓↓ | 2.2 x 10-7 |
| cg25542319 | 5 | 112540429 |  | MCC | Body | ↑↑ | 2.2 x 10-7 |
| cg14983362 | 11 | 118901610 | Island | SLC37A4 | 1stExon,  5'UTR,  TSS1500 | ↑↑ | 2.8 x 10-7 |
| cg17442683 | 1 | 8664311 |  | RERE | Body | ↑↑ | 3.5 x 10-7 |
| cg06673536 | 19 | 45213941 | Shelf | CEACAM16 | 3'UTR | ↓↓ | 3.7 x 10-7 |
| cg10753966 | 3 | 55556197 |  | ERC2 | 3'UTR | ↑↑ | 4.0 x 10-7 |
| cg05099952 | 16 | 30367546 | Shore | CD2BP2 | TSS1500 | ↓↓ | 4.2 x 10-7 |
| cg07580762 | 1 | 161171810 | Island | NDUFS2 | 5'UTR,  TSS200 | ↑↑ | 4.8 x 10-7 |
| cg16423910 | 19 | 49843627 | Island | CD37 | 3'UTR | ↓↓ | 5.5 x 10-7 |
| cg06383241 | 12 | 116997022 |  | MAP1LC3B2 | TSS200 | ↓↓ | 5.7 x 10-7 |
| cg19270739 | 1 | 1368846 | Shore |  |  | ↓↓ | 5.9 x 10-7 |
| cg02314339 | 10 | 91020653 |  |  |  | ↑↑ | 6.0 x 10-7 |
| cg14583825 | 19 | 54393040 | Island | PRKCG | Body | ↓↓ | 7.1 x 10-7 |
| cg14580628 | 5 | 43602116 | Shore | NNT | TSS1500 | ↓↓ | 7.9 x 10-7 |
| cg06186150 | 1 | 2458298 | Shore | PANK4 | TSS1500 | ↑↑ | 8.3 x 10-7 |
| cg02158978 | 12 | 133134938 | Shore | FBRSL1 | Body | ↓↓ | 8.4 x 10-7 |
| cg24262469 | 3 | 156391694 | Shore | TIPARP /  LOC100287227 | TSS1500 /  Body | ↑↑ | 8.6 x 10-7 |
| cg04246167 | 3 | 58984465 |  | C3orf67 | 5'UTR | ↓↓ | 8.7 x 10-7 |
| cg20697394 | 12 | 132918305 | Shelf |  |  | ↓↓ | 9.3 x 10-7 |
| cg16313343 | 14 | 105768109 | Shore | BRF1 | TSS1500 | ↓↓ | 1.0 x 10-6 |
| cg07568588 | 1 | 88338001 |  |  |  | ↓↓ | 1.0 x 10-6 |
| cg07240000 | 1 | 17878538 |  | ARHGEF10L | 5'UTR | ↓↓ | 1.1 x 10-6 |
| cg20433952 | 17 | 55607898 |  | MSI2 | Body | ↓↓ | 1.2 x 10-6 |
| cg14430937 | 12 | 120729982 |  |  |  | ↑↑ | 1.2 x 10-6 |
| cg05824218 | 17 | 38499096 | Shore | RARA | 1stExon,  Body | ↓↓ | 1.2 x 10-6 |
| cg04605617 | 1 | 20501558 |  | PLA2G2C | 1stExon | ↑↑ | 1.2 x 10-6 |
| cg22325145 | 22 | 38825918 | Shore | KCNJ4 | 5'UTR | ↓↓ | 1.2 x 10-6 |
| cg03460109 | 4 | 7427313 |  | SORCS2 | Body | ↓↓ | 1.2 x 10-6 |
| cg12731773 | 11 | 846055 | Shelf | TSPAN4 | 5'UTR | ↓↓ | 1.2 x 10-6 |
| cg25260176 | 12 | 57569940 | Island | LRP1 | Body | ↓↓ | 1.3 x 10-6 |
| cg08677954 | 6 | 31604108 |  | BAT2 | Body | ↑↑ | 1.5 x 10-6 |
| cg08684991 | 12 | 11662075 |  |  |  | ↓↓ | 1.5 x 10-6 |
| cg10959408 | 1 | 54017944 |  | GLIS1 | Body | ↓↓ | 1.6 x 10-6 |
| cg10250177 | 1 | 32739752 | Shore | LCK | 5'UTR,  1stExon | ↓↓ | 1.7 x 10-6 |
| cg07252792 | 22 | 21987048 | Shelf | CCDC116 | TSS200 | ↓↓ | 1.8 x 10-6 |
| cg11152412 | 15 | 74927688 |  | EDC3 | Body | ↑↑ | 1.9 x 10-6 |
| cg27554551 | 16 | 4421486 | Shore | VASN /  CORO7 | TSS1500 /  Body | ↓↓ | 1.9 x 10-6 |
| cg10817916 | 17 | 61511069 | Shore | CYB561 | 3'UTR | ↓↓ | 2.1 x 10-6 |
| cg18394552 | 5 | 159428643 |  |  |  | ↓↓ | 2.2 x 10-6 |
| cg01806956 | 1 | 9460830 |  |  |  | ↓↓ | 2.3 x 10-6 |
| cg03221025 | 16 | 88955224 | Shore | CBFA2T3 | Body | ↓↓ | 2.4 x 10-6 |
| cg22603569 | 19 | 3388047 | Island | NFIC | Body | ↓↓ | 2.5 x 10-6 |
| cg00022866 | 11 | 64108440 | Shore | CCDC88B | Body | ↓↓ | 2.5 x 10-6 |
| cg10139742 | 16 | 56352151 |  | GNAO1 | Body | ↑↑ | 2.8 x 10-6 |
| cg08217545 | 19 | 3388013 | Island | NFIC | Body | ↓↓ | 2.8 x 10-6 |
| cg25737313 | 19 | 12899557 | Shore |  |  | ↓↓ | 2.9 x 10-6 |
| cg08227353 | 10 | 102821670 | Island | KAZALD1 | 1stExon,  5'UTR | ↓↓ | 3.1 x 10-6 |
| cg17934790 | 19 | 14693742 |  | CLEC17A | TSS200 | ↓↓ | 3.1 x 10-6 |
| cg06121226 | 4 | 72134060 |  | SLC4A4 | Body | ↓↓ | 3.2 x 10-6 |
| cg07262457 | 3 | 128777371 |  |  |  | ↓↓ | 3.3 x 10-6 |
| cg19046904 | 22 | 46426201 | Shelf |  |  | ↓↓ | 3.3 x 10-6 |
| cg07121900 | 13 | 50706912 | Shore |  |  | ↑↑ | 3.4 x 10-6 |
| cg17897187 | 1 | 14923736 | Shore | KIAA1026 | TSS1500 | ↑↑ | 3.4 x 10-6 |
| cg08241514 | 22 | 50438769 | Island | IL17REL | Body | ↓↓ | 3.4 x 10-6 |
| cg02856716 | 1 | 18993307 |  | PAX7 | Body | ↓↓ | 3.4 x 10-6 |
| cg11024682 | 17 | 17730094 | Shelf | SREBF1 | Body | ↓↓ | 3.5 x 10-6 |
| cg04418434 | 6 | 7110773 | Shore | RREB1 | 5'UTR | ↑↑ | 3.6 x 10-6 |
| cg25881170 | 3 | 107810507 | Island | CD47 | TSS1500 | ↑↑ | 3.6 x 10-6 |
| cg21691116 | 1 | 161171819 | Island | NDUFS2 | 5'UTR,  TSS200 | ↑↑ | 3.7 x 10-6 |
| cg24251439 | 19 | 1112327 | Island | SBNO2 | Body | ↓↓ | 3.8 x 10-6 |
| cg08810397 | 16 | 1521676 | Shelf | CLCN7 | Body | ↓↓ | 4.0 x 10-6 |
| cg02159996 | 6 | 89927233 |  | GABRR1 | 5'UTR,  1stExon | ↓↓ | 4.0 x 10-6 |
| cg14165660 | 10 | 112889349 |  |  |  | ↓↓ | 4.1 x 10-6 |
| cg23006567 | 19 | 53966842 | Shelf |  |  | ↓↓ | 4.1 x 10-6 |
| cg14320320 | 3 | 16577787 |  |  |  | ↓↓ | 4.1 x 10-6 |
| cg15096140 | 2 | 192109731 | Shore | MYO1B | TSS1500 | ↑↑ | 4.2 x 10-6 |
| cg24906420 | 12 | 133133512 | Shore | FBRSL1 | Body | ↓↓ | 4.2 x 10-6 |
| cg19753867 | 20 | 35383166 |  | DSN1 | Body | ↑↑ | 4.2 x 10-6 |
| cg12232388 | 12 | 125027851 | Shore |  |  | ↓↓ | 4.3 x 10-6 |
| cg16049890 | 5 | 139123186 | Shelf |  |  | ↓↓ | 4.4 x 10-6 |
| cg22360765 | 2 | 47298563 |  | TTC7A | Body | ↑↑ | 4.6 x 10-6 |
| cg20692268 | 1 | 25358981 |  |  |  | ↓↓ | 4.8 x 10-6 |
| cg27521562 | 17 | 1107460 | Shore |  |  | ↓↓ | 4.8 x 10-6 |
| cg20589883 | 4 | 111115135 | Shelf | ELOVL6 | Body | ↓↓ | 4.9 x 10-6 |
| cg15501231 | 6 | 31737630 |  | C6orf27 | Body | ↓↓ | 5.1 x 10-6 |
| cg06369349 | 19 | 49503178 |  | RUVBL2 | Body | ↑↑ | 5.4 x 10-6 |
| cg24686236 | 5 | 14323412 |  | TRIO | Body | ↓↓ | 5.5 x 10-6 |
| cg16688112 | 16 | 88922774 | Island | GALNS /  TRAPPC2L | Body /  TSS1500 | ↓↓ | 5.7 x 10-6 |
| cg01695994 | 17 | 80246403 | Shelf |  |  | ↓↓ | 6.0 x 10-6 |
| cg05655534 | 2 | 62798448 |  |  |  | ↑↑ | 6.1 x 10-6 |
| cg09766547 | 7 | 30465150 |  | NOD1 | 3'UTR | ↓↓ | 6.1 x 10-6 |
| cg14176088 | 1 | 9785289 |  | PIK3CD | Body | ↑↑ | 6.3 x 10-6 |
| cg18642369 | 13 | 99651231 |  | DOCK9 | Body | ↑↑ | 6.4 x 10-6 |
| cg03031932 | 16 | 81547138 |  | CMIP | Body | ↓↓ | 6.6 x 10-6 |
| cg17176619 | 13 | 99218657 |  | STK24 | Body | ↑↑ | 6.6 x 10-6 |
| cg01008405 | 5 | 139039026 | Shore | CXXC5 | 5'UTR | ↓↓ | 6.7 x 10-6 |
| cg07286682 | 15 | 69447132 |  | MIR548H4 | Body | ↓↓ | 7.2 x 10-6 |
| cg02873991 | 12 | 25151263 |  | C12orf77 | TSS1500 | ↓↓ | 7.3 x 10-6 |
| cg10816760 | 6 | 142890973 |  | LOC153910 | Body | ↓↓ | 7.5 x 10-6 |
| cg26906737 | 1 | 212541551 |  | TMEM206 | Body | ↑↑ | 7.6 x 10-6 |
| cg20793420 | 22 | 38861635 | Shelf |  |  | ↓↓ | 7.6 x 10-6 |
| cg12746706 | 6 | 169276508 |  |  |  | ↓↓ | 7.6 x 10-6 |
| cg16743273 | 19 | 2076833 | Island | MOBKL2A | Body | ↓↓ | 7.6 x 10-6 |
| cg04193083 | 17 | 41323562 | Shore | NBR1 | 5'UTR | ↑↑ | 7.7 x 10-6 |
| cg11992015 | 2 | 110876674 | Shelf |  |  | ↑↑ | 7.9 x 10-6 |
| cg08530064 | 7 | 150598393 |  |  |  | ↓↓ | 7.9 x 10-6 |
| cg23889047 | 1 | 7705756 |  | CAMTA1 | Body | ↓↓ | 8.3 x 10-6 |
| cg11831006 | 3 | 125100635 |  |  |  | ↓↓ | 8.4 x 10-6 |
| cg24539599 | 5 | 112824920 | Shore | MCC | TSS1500 | ↑↑ | 8.9 x 10-6 |
| cg09742751 | 20 | 16553921 | Island | KIF16B | 1stExon,  5'UTR | ↓↓ | 9.0 x 10-6 |
| cg09449232 | 12 | 106135284 |  |  |  | ↑↑ | 9.2 x 10-6 |
| cg00591660 | 16 | 2478353 | Shore | CCNF | TSS1500 | ↓↓ | 9.4 x 10-6 |
| cg08949143 | 13 | 30947713 |  | LOC100188949 | Body | ↓↓ | 9.5 x 10-6 |
| cg02402423 | 19 | 41255444 | Shore | C19orf54 /  SNRPA | 1stExon /  TSS1500 | ↓↓ | 9.7 x 10-6 |
| cg26354367 | 6 | 30010457 |  | NCRNA00171 | Body | ↓↓ | 9.7 x 10-6 |
| cg13271643 | 13 | 21036583 |  | CRYL1 | Body | ↓↓ | 9.9 x 10-6 |
| cg16417374 | 1 | 26098310 | Shore | MAN1C1 | Body | ↓↓ | 1.0 x 10-5 |
| cg22563815 | 15 | 78856949 | Shore | CHRNA5 | TSS1500 | ↓↓ | 1.1 x 10-5 |
| cg17861836 | 17 | 79202505 |  | C17orf56 | 3'UTR | ↓↓ | 1.1 x 10-5 |
| cg23907108 | 11 | 64405993 | Island | NRXN2 | Body | ↑↑ | 1.1 x 10-5 |
| cg05018460 | 15 | 80688078 |  |  |  | ↑↑ | 1.1 x 10-5 |
| cg16668176 | 19 | 5308893 |  | PTPRS | 5'UTR | ↓↓ | 1.1 x 10-5 |
| cg20429981 | 1 | 1609972 | Shore | CDK11B /  LOC728661 | Body,  5'UTR /  5'UTR | ↓↓ | 1.1 x 10-5 |
| cg01994902 | 16 | 1576069 | Shore | IFT140 | Body | ↓↓ | 1.2 x 10-5 |
| cg07870074 | 10 | 706006 |  | DIP2C /  C10orf108 | Body /  Body | ↓↓ | 1.2 x 10-5 |
| cg00129811 | 6 | 116726398 |  | DSE | Body | ↓↓ | 1.3 x 10-5 |
| cg15226659 | 19 | 4552594 | Island | SEMA6B | Body | ↓↓ | 1.3 x 10-5 |
| cg22617002 | 13 | 112275633 | Island |  |  | ↓↓ | 1.4 x 10-5 |
| cg22137772 | 3 | 150755800 |  | CLRN1OS | Body | ↓↓ | 1.4 x 10-5 |
| cg05048624 | 1 | 20441579 |  | PLA2G2D | Body | ↓↓ | 1.4 x 10-5 |
| cg08417595 | 19 | 3811002 | Island | ZFR2 | Body | ↓↓ | 1.4 x 10-5 |
| cg13800769 | 12 | 4916913 | Shore | KCNA6 | TSS1500 | ↓↓ | 1.4 x 10-5 |
| cg04514392 | 3 | 107086058 |  |  |  | ↓↓ | 1.4 x 10-5 |
| cg20421058 | 4 | 7337225 |  | SORCS2 | Body | ↓↓ | 1.4 x 10-5 |
| cg22001211 | 2 | 61766532 | Shore | XPO1 | TSS1500 | ↓↓ | 1.5 x 10-5 |
| cg18753841 | 11 | 8680469 |  | TRIM66 | TSS200 | ↑↑ | 1.5 x 10-5 |
| cg21646084 | 2 | 16802843 |  | FAM49A | 5'UTR | ↓↓ | 1.5 x 10-5 |
| cg08817422 | 6 | 30654638 | Island | KIAA1949 | 5'UTR,  1stExon | ↓↓ | 1.5 x 10-5 |
| cg21896766 | 8 | 114444395 | Shore | CSMD3 | Body | ↑↑ | 1.6 x 10-5 |
| cg11793449 | 17 | 76313872 | Shelf |  |  | ↓↓ | 1.6 x 10-5 |
| cg01616876 | 12 | 113544928 | Shelf | RASAL1 | Body | ↓↓ | 1.6 x 10-5 |
| cg16163382 | 2 | 37938640 |  |  |  | ↓↓ | 1.6 x 10-5 |
| cg17375396 | 11 | 67202808 | Shore | RPS6KB2 | 3'UTR | ↓↓ | 1.6 x 10-5 |
| cg19377250 | 7 | 100463206 | Shore | SLC12A9 | Body | ↓↓ | 1.6 x 10-5 |
| cg07528595 | 12 | 54814557 | Shore |  |  | ↓↓ | 1.7 x 10-5 |
| cg24712249 | 1 | 155830294 | Island | SYT11 | Body | ↓↓ | 1.7 x 10-5 |
| cg06827038 | 17 | 48912952 |  | WFIKKN2 | 1stExon,  5'UTR | ↓↓ | 1.7 x 10-5 |
| cg01154283 | 2 | 36603543 |  | CRIM1 | Body | ↓↓ | 1.7 x 10-5 |
| cg13148151 | 3 | 45637978 | Shelf | LIMD1 | Body | ↓↓ | 1.7 x 10-5 |
| cg26829395 | 15 | 40217855 |  |  |  | ↓↓ | 1.7 x 10-5 |
| cg17743381 | 1 | 39024825 |  |  |  | ↓↓ | 1.8 x 10-5 |
| cg08977611 | 20 | 42953248 | Shelf |  |  | ↓↓ | 1.8 x 10-5 |
| cg00013899 | 1 | 64992433 |  | CACHD1 | Body | ↓↓ | 1.9 x 10-5 |
| cg13729816 | 19 | 52954722 | Island |  |  | ↓↓ | 1.9 x 10-5 |
| cg21900616 | 22 | 20286845 | Island |  |  | ↓↓ | 1.9 x 10-5 |
| cg00722097 | 6 | 111195976 | Island | AMD1 | TSS200 | ↓↓ | 2.0 x 10-5 |
| cg24277586 | 3 | 52099561 |  | C3orf74 | TSS1500 | ↓↓ | 2.0 x 10-5 |
| cg05483509 | 16 | 2563435 | Island | ATP6V0C | TSS1500 | ↓↓ | 2.0 x 10-5 |
| cg07636952 | 10 | 124596397 |  | CUZD1 | Body | ↑↑ | 2.1 x 10-5 |
| cg08986840 | 8 | 38409865 |  |  |  | ↓↓ | 2.1 x 10-5 |
| cg04202267 | 2 | 169431900 |  | LASS6 | Body | ↓↓ | 2.1 x 10-5 |
| cg18132851 | 6 | 152085641 |  | ESR1 | 5'UTR | ↑↑ | 2.1 x 10-5 |
| cg19507267 | 3 | 108896930 |  | C3orf66 | TSS200 | ↓↓ | 2.1 x 10-5 |
| cg14588606 | 17 | 39183560 |  | KRTAP1-5 | TSS200 | ↑↑ | 2.2 x 10-5 |
| cg20729813 | 4 | 7502429 |  | SORCS2 | Body | ↑↑ | 2.3 x 10-5 |
| cg15033653 | 12 | 113587581 | Shelf | CCDC42B | TSS200 | ↓↓ | 2.3 x 10-5 |
| cg05339515 | 16 | 68624615 |  |  |  | ↑↑ | 2.3 x 10-5 |
| cg10529613 | 14 | 25287305 |  | STXBP6 | Body | ↓↓ | 2.4 x 10-5 |
| cg25921609 | 17 | 8379225 | Shore | MYH10 | Body | ↓↓ | 2.4 x 10-5 |
| cg14172849 | 14 | 104171259 |  | XRCC3 | Body | ↓↓ | 2.4 x 10-5 |
| cg12464638 | 11 | 844400 | Shore | TSPAN4 | TSS200,  5'UTR | ↓↓ | 2.4 x 10-5 |
| cg27064708 | 14 | 69030612 |  | RAD51L1 | Body | ↓↓ | 2.5 x 10-5 |
| cg04929932 | 1 | 91195683 | Shelf |  |  | ↑↑ | 2.5 x 10-5 |
| cg21807240 | 14 | 23425770 | Shore | HAUS4 | 5'UTR | ↓↓ | 2.6 x 10-5 |
| cg04331601 | 19 | 17633880 | Shore | FAM129C | TSS1500 | ↓↓ | 2.6 x 10-5 |
| cg17744604 | 1 | 206946166 |  | IL10 | TSS1500 | ↓↓ | 2.6 x 10-5 |
| cg01881062 | 1 | 6660403 | Shore | KLHL21 | Body | ↓↓ | 2.6 x 10-5 |
| cg22356061 | 1 | 227954102 |  | SNAP47 | Body | ↓↓ | 2.6 x 10-5 |
| cg16808156 | 20 | 3835875 |  | MAVS | Body | ↑↑ | 2.6 x 10-5 |
| cg13543355 | 14 | 77350013 |  |  |  | ↓↓ | 2.6 x 10-5 |
| cg20629315 | 2 | 43685377 |  | THADA | Body | ↓↓ | 2.7 x 10-5 |
| cg27016544 | 17 | 10002002 |  | GAS7 | Body | ↓↓ | 2.7 x 10-5 |
| cg13357922 | 10 | 135251512 | Shelf |  |  | ↑↑ | 2.7 x 10-5 |
| cg14211332 | 1 | 117255389 |  |  |  | ↑↑ | 2.7 x 10-5 |
| cg27572855 | 1 | 25598939 |  | RHD | TSS200 | ↓↓ | 2.8 x 10-5 |
| cg05708512 | 5 | 31731391 |  |  |  | ↓↓ | 2.8 x 10-5 |
| cg25598890 | 12 | 117501447 |  | TESC | Body | ↓↓ | 2.8 x 10-5 |
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| **eTable 3.** Summary of sensitivity analyses of arsenic-associated CpG sites discovered in meta-analysis. | | | | | | |
|  | **Cohort** | **Consistenta** | **Inconsistentb** | **Pc** | **% Consistent** |
| ln(DMA)d | HEALS | 146 | 75 | 1.0 x 10-6 | 66.1% |
| MR Max-Likelihoode | Combined | 134 | 87 | 9.5 x 10-4 | 60.6% |
| Binary SNP Scoref,g | Combined | 148 | 73 | 2.5 x 10-7 | 67.0% |
| aNumber of associations with methylations of CpG sites that are opposite in sign from arsenic exposure associations.  bSame sign as arsenic exposure associations.  cRelative to the null hypothesis that signs of associations among the set of 221 CpGs do not tend to be consistent with arsenic exposure associations. Reported one-sided p-values.  dCpG methylation ~ ln(DMA) + age + sex + methylation batch + smoking status + BMI + education + ln(water As) + ln(urine As) + ln(urine creatinine).  eMaximum likelihood Mendelian randomization  fCpG methylation ~ binary SNP score + age + sex + methylation batch + smoking status  gCoded as a binary variable indicating 2 copies of the effect allele for both rs9527 and rs61735836. | | | | | | |

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| **eTable 4.** Summary of cohort-stratified analyses of arsenic-associated CpG sites discovered in meta-analysis. | | | | | | |
|  | **Cohort** | **Consistenta** | **Inconsistentb** | **Pc** | **% Consistent** |
| Weighted GP-DMA%d | HEALS | 130 | 91 | 5.2 x 10-3 | 58.8% |
|  | BEST | 134 | 87 | 9.5 x 10-4 | 60.6% |
| Binary SNP Scoree,f | HEALS | 146 | 75 | 1.0 x 10-6 | 66.1% |
|  | BEST | 108 | 113 | 6.6 x 10-1 | 48.9% |
| MR-IVWg | HEALS | 131 | 90 | 3.5 x 10-3 | 59.3% |
|  | BEST | 134 | 87 | 1.0 x 10-3 | 60.6% |

aNumber of associations with methylations of CpG sites that are opposite in sign from arsenic exposure associations.

bSame sign as arsenic exposure associations.

cRelative to the null hypothesis that signs of associations among the set of 221 CpGs do not tend to be consistent with arsenic exposure associations. Reported one-sided p-values.

dCpG methylation ~ weighted GP-DMA% + age + sex + methylation batch + smoking status

eCpG methylation ~ binary SNP score + age + sex + methylation batch + smoking status

fCoded as a binary variable indicating 2 copies of the effect allele for both rs9527 and rs61735836.

gInverse-variance weighted Mendelian randomization

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| **eTable 5.** Summary of analyses of CpG sites discovered in meta-analysis associated with arsenic based on a Bonferroni P-value threshold. | | | | | | |
|  | **Cohort** | **Consistenta** | **Inconsistentb** | **Pc** | **% Consistent** |
| Weighted GP-DMA%d | Combined | 29 | 12 | 5.8 x 10-3 | 70.7% |
| Binary SNP Scoree,f | Combined | 32 | 9 | 2.2 x 10-4 | 78.0% |
| MR-IVWg | Combined | 27 | 14 | 3.0 x 10-2 | 65.9% |

aNumber of associations with methylations of CpG sites that are opposite in sign from arsenic exposure associations.

bSame sign as arsenic exposure associations.

cRelative to the null hypothesis that signs of associations among the set of 41 CpGs do not tend to be consistent with arsenic exposure associations. Reported one-sided p-values.

dCpG methylation ~ weighted GP-DMA% + age + sex + methylation batch + smoking status

eCpG methylation ~ binary SNP score + age + sex + methylation batch + smoking status

fCoded as a binary variable indicating 2 copies of the effect allele for both rs9527 and rs61735836.

gInverse-variance weighted Mendelian randomization

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| **eTable 6.** Summary of individual SNP analyses of arsenic-associated CpG sites discovered in meta-analysis. | | | | | | |
|  | **Cohort** | **Consistenta** | **Inconsistentb** | **Pc** | **% Consistent** |
| rs9527d,f | HEALS | 108 | 113 | 6.6 x 10-1 | 48.9% |
|  | Combined | 132 | 89 | 2.3 x 10-3 | 59.7% |
| rs11191527e,f | HEALS | 94 | 127 | 9.9 x 10-1 | 42.5% |
|  | Combined | 120 | 101 | 1.1 x 10-1 | 54.3% |
| rs61735836d,g | HEALS | 136 | 85 | 3.7 x 10-4 | 61.5% |
|  | Combined | 131 | 90 | 3.5 x 10-3 | 59.3% |
| aNumber of associations with methylations of CpG sites that are opposite in sign from arsenic exposure associations.  bSame sign as arsenic exposure associations.  cRelative to the null hypothesis that signs of associations among the set of 41 CpGs do not tend to be consistent with arsenic exposure associations. Reported one-sided p-values.  dCoded as a binary variable indicating 2 copies of effect allele.  eCoded as a binary variable indicating 1 or 2 copies of effect allele.  fCpG methylation ~ rs9527 + rs11191527 + age + sex + methylation batch + smoking status  gCpG methylation ~ rs61735836 + age + sex + methylation batch + smoking status | | | | | | |

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| **eTable 7.** Summary of analyses of arsenic-associated CpG sites discovered in HEALS. | | | | | | |
|  | **Cohort** | **Consistenta** | **Inconsistentb** | **Pc** | **% Consistent** |
| DMA%d | HEALS | 22 | 12 | 6.1 x 10-2 | 64.7% |
| ln(DMA)e | HEALS | 24 | 10 | 1.2 x 10-2 | 70.6% |
| Weighted GP-DMA%f | HEALS | 23 | 11 | 2.9 x 10-2 | 67.6% |
| Binary SNP Scoreg,h | HEALS | 27 | 7 | 4.0 x 10-4 | 79.0% |
| MR-IVWi | HEALS | 25 | 9 | 4.5 x 10-3 | 73.5% |

aNumber of associations with methylations of CpG sites that are opposite in sign from arsenic exposure associations.

bSame sign as arsenic exposure associations.

cRelative to the null hypothesis that signs of associations among the set of 34 CpGs do not tend to be consistent with arsenic exposure associations. Reported one-sided p-values.

dCpG methylation ~ DMA% + age + sex + methylation batch + smoking status + BMI + education + ln(water As)

eCpG methylation ~ ln(DMA) + age + sex + methylation batch + smoking status + BMI + education + ln(water As) + ln(urine As) + ln(urine creatinine).

fCpG methylation ~ weighted GP-DMA% + age + sex + methylation batch + smoking status

gCpG methylation ~ binary SNP score + age + sex + methylation batch + smoking status

hCoded as a binary variable indicating 2 copies of the effect allele for both rs9527 and rs61735836.

iInverse-variance weighted Mendelian randomization

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| **eFigure 1. DMA% and ln(DMA) versus arsenic exposure in HEALS participants (n=383).** Pearson correlations and corresponding p-values were reported. | |

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| **eFigure 2. Associations of ln(DMA) with DNA methylation at 221 arsenic-associated CpGs discovered in meta-analysis.** The study population was HEALS (*n* = 379). |

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| **eFigure 3. Associations of binary SNP score with DNA methylation at 221 arsenic-associated CpGs discovered in meta-analysis.** The study population was the combined HEALS and BEST cohort (*n* = 772). |

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| A | B |
| C | D |
| E | F |
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| **eFigure 4. Mendelian randomization and forest plots for CpGs with strongest effect estimates**. (A-B) cg18050715, (C-D) cg04826368, (E-F) cg14583825. (A, C, E) Horizontal and vertical error bars represent the 95% CI for the β coefficient of each SNP’s association with DMA% and CpG methylation, respectively. (B, D, F) Horizontal lines represent the 95% CI for β coefficient of each SNP’s association with CpG methylation. | |

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| A |
| B |
| C |
| **eFigure 5. Associations of each SNP genotype with DNA methylation at 221 arsenic-associated CpGs discovered in meta-analysis.** (A) rs9527, (B) rs11191527, and (C) rs61735836. Study populations were a combined cohort of HEALS and BEST (*n* = 772) for rs9527 and rs11191527, and a subset of the combined cohort with full genotypic data (*n* = 723) for rs61735836. |