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# Repeat measures of DNA methylation in an inception cohort of firefighters

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## ABSTRACT

**Objectives** Firefighters face exposures associated with adverse health outcomes including risk for multiple cancers. DNA methylation, one type of epigenetic regulation, provides a potential mechanism linking occupational hazards to adverse health outcomes. We hypothesised that DNA methylation profiles would change in firefighters after starting their service and that these patterns would be associated with occupational exposures (cumulative fire-hours and fire-runs).

**Methods** We profiled DNA methylation with the Infinium MethylationEPIC in blood leucocytes at two time points in non-smoking new recruits: prior to live fire training and 20–37 months later. Linear mixed effects models adjusted for potential confounders were used to identify differentially methylated CpG sites over time using data from 50 individuals passing all quality control.

**Results** We report 680 CpG sites with altered methylation (q value <0.05) including 60 with at least a 5% methylation difference at follow-up. Genes with differentially methylated CpG sites were enriched in biological pathways related to cancers, neurological function, cell signalling and transcription regulation. Next, linear mixed effects models were used to determine associations between occupational exposures with methylation at the 680 loci. Of these, more CpG sites were associated with fire-runs (108 for all and 78 for structure-fires only, q<0.05) than with fire-hours (27 for all fires and 1 for structure fires). These associations were independent of time since most recent fire, suggesting an impact of cumulative exposures.

**Conclusions** Overall, this study provides evidence that DNA methylation may be altered by fireground exposures, and the impact of this change on disease development should be evaluated.

## INTRODUCTION

The fire service is an essential workforce, yet firefighters face occupational hazards including chemical exposures, heat stress, circadian disruptions and mental stressors. Some combustion byproducts that firefighters are exposed to are known or suspected human carcinogens.<sup>1,2</sup> There is evidence for increased overall risk of cancer incidence and mortality when comparing US firefighters to the general population.<sup>3,4</sup> In 2010, a working group of the International Agency of Research on Cancer designated the firefighting occupation as a Group 2B carcinogen, indicating it is possibly carcinogenic to humans but evidence to complete the evaluation was limited.<sup>2</sup> Firefighting exposures have also been

## Key messages

### What is already known about this subject?

- ⇒ DNA methylation is an epigenetic regulator that is responsive to hazardous environmental exposures, including exposures that firefighters face in the workplace.
- ⇒ Changes in DNA methylation contribute to the development of many diseases including cancers.

### What are the new findings?

- ⇒ DNA methylation changed at 680 sites throughout the genome in new firefighters when comparing baseline samples to samples collected after 20–37 months of working.
- ⇒ Proxies for fireground exposures were associated with DNA methylation at 140 of these sites.
- ⇒ These sites were in genes related to cancers, immune function and other disease pathways.

### How might this impact on policy or clinical practice in the foreseeable future?

- ⇒ DNA methylation changes occur before disease develops.
- ⇒ DNA methylation profiles could be used to inform occupational risk assessment for firefighters.
- ⇒ They could also be developed into biomarkers to screen for professionals most at risk for adverse health outcomes that would benefit from prevention efforts.

associated with death from cardiovascular disease, adverse mental health outcomes and injuries.<sup>5–7</sup>

Diseases linked to chronic firefighting exposures may take decades to develop. It is difficult to accurately assess occupational health risks and to implement appropriate prevention and intervention strategies to protect firefighter health given this timeline. Molecular biomarkers, such as epigenetics, reflect subtle biological changes that occur following exposures that contribute to subsequent disease risk and development. The epigenome consists of modifications to DNA and chromatin that do not alter the underlying DNA sequence. One major type of epigenetic regulation is DNA methylation, which is fairly stable across time and often represses gene expression, especially when in the promoter region of genes.<sup>8</sup> Epigenetic



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modifications are responsive to the environment, and reproducible epigenetic signatures of exposures such as cigarette smoking have been identified.<sup>9–10</sup> Epigenetic perturbations are thought to underlie many human diseases.<sup>11</sup> Epigenetic alterations contribute mechanistically to the hallmarks of cancer,<sup>12</sup> and are also one of 10 key characteristics by which carcinogens may exert their effects.<sup>13</sup> Thus, profiling epigenetic marks in firefighters could serve as biomarkers of cumulative exposures and elucidate in which gene pathways DNA methylation is changing.

We have previously shown differential blood DNA methylation in incumbent compared with new recruit firefighters, adjusted for age and other covariates. Differentially methylated loci between the two groups were in genes previously linked to cancer—*YIPF6*, *MPST* and *PCED1B*.<sup>14</sup> However, this study was limited by comparing new recruits and incumbents sampled at one time point each without data on the incumbents' pre-firefighting epigenetic profiles. We also evaluated associations between exposures to perfluoroalkyl and polyfluoroalkyl substances (PFAS), one of the many chemical classes to which firefighters can be occupationally exposed, with DNA methylation among structural firefighters. We reported statistically significant associations between several PFAS with accelerated epigenetic age and altered DNA methylation at cancer-function and immune-function related genes.<sup>15</sup> However, these previous studies were limited by lack of access to the baseline pre-firefighting epigenetic profiles.

In terms of other biomarkers, we have identified whole blood microRNA (miRNA) expression at cancer-linked miRNAs when comparing new recruits to incumbents<sup>16</sup> and in a longitudinal design comparing matched baseline to follow-up samples from new firefighters.<sup>17</sup> In general, miRNAs with tumour suppressor activity were decreased and miRNAs with oncogenic activity were increased in incumbent firefighters and in follow-up samples from the new firefighters. In addition, in the follow-up sample analysis in the new firefighters some miRNAs were associated with cumulative measures of fireground exposure and also with time since most recent fire. We have designed the current study to investigate changes to DNA methylation profiles in a similar manner to assess whether the methylation status of any genes are associated with chronic fireground exposures, even within a short time of follow-up. The type of fireground exposure—structure fires compared with vehicle, outdoor or other fire types—may also be important in this association. For example, median urinary concentrations of polycyclic aromatic hydrocarbon (PAH) metabolites measured after a fire response were greatest among firefighters who performed interior operations at structural fires.<sup>18</sup>

In this study, we profiled DNA methylation in non-smoking new recruits prior to live fire training and again 20–37 months later in blood leucocyte samples via the Infinium MethylationEPIC.<sup>19</sup> We compared DNA methylation profiles at baseline and follow-up, and assessed associations between proxies of occupational exposure (cumulative fire-hours and fire-runs for all fires and structure fires-only) at loci that changed over time. We hypothesised that differentially methylated genes would have functions relevant to carcinogenesis or response to environmental exposures and that DNA methylation patterns would exhibit a dose–response relationship with proxies of cumulative exposure.

## METHODS

### Cohort recruitment and study population

New firefighters ('recruits') with no previous live-fire exposures were enrolled from the Tucson Fire Department (Arizona, USA) between 2015 and 2016.<sup>17</sup> Demographics (age, ethnicity, race), height and weight, and current tobacco usage were assessed via

a questionnaire at study enrolment ('baseline'). A follow-up visit was conducted 20–37 months later, and the time in between is herein referred to as the length of service.

Blood samples for DNA methylation measurements were collected at the baseline and follow-up visits by qualified phlebotomists into dipotassium ethylenediaminetetraacetic acid tubes (K2-EDTA; Beckton, Dickinson and Company, Franklin Lakes, New Jersey, USA), and stored frozen until use.<sup>14</sup>

To be included in the analyses described in this paper, participants had to: (1) be new firefighters at baseline, (2) complete both baseline and follow-up visits, (3) provide data on all key covariates, (4) report no tobacco usage at the baseline visit and (5) provide blood samples at baseline prior to live-fire training and at follow-up for DNA methylation analysis. Out of 90 new recruits from 2015 and 2016, 88 (98%) chose to enrol. Of the 76 who had blood drawn prior to live-fire training at baseline, 17 either did not finish recruit training or left the Tucson Fire Department prior to follow-up, 2 declined follow-up participation and 55 completed their follow-up by the time of DNA methylation analysis and met all other inclusion criteria. Of these, 5 failed quality control for at least one of their samples and were excluded from data analysis for a final set of 50 firefighters with data at baseline and follow-up.

### Measures of fireground exposures

We collected data from the fire department's response records to compute cumulative hours at fires (fire-hours) and cumulative number of fires (fire-runs) that each individual experienced between baseline and follow-up.<sup>17</sup> The records include information on type of fire, date, time and duration of fire response (in minutes). Here we define a fire-run as responding to one fire (any type of any duration). We computed fire-hours and fire-runs for both all fire types and structure fires only. Fire-runs and fire-hours have been used as measures of cumulative fireground exposure in previous research.<sup>17–20</sup> We calculated time since most recent fire (in days), using the date of the last fire-run and the date of sample collection, as a proxy for recent/acute exposures.

### DNA methylation analysis

DNA was isolated from blood leucocytes, and concentration was measured via a QuantiFluor dsDNA System (Promega) or a Qubit Fluorometer (Thermo Scientific). DNA methylation was quantified using the Infinium MethylationEPIC array<sup>19</sup> following bisulfite conversion via Zymo EZ-96 DNA Methylation kits. Full details on laboratory procedures for this analysis and preprocessing of the data can be found in online supplemental methods.

### Statistical analysis

All data preprocessing and statistical analyses were conducted in the R Project for Statistical Computing (version  $\geq 4.00.3$ ). Descriptive statistics were calculated and compared between baseline and follow-up when appropriate using *t*-tests or  $\chi^2$  tests. Singular value decomposition analysis was performed to identify technical and biological covariates that correlate strongly with variation in the DNA methylation data.<sup>21</sup> Cell type proportions, PC representing technical variation and pack-year residuals strongly correlated with DNA methylation.

We first used linear mixed models to identify CpG sites differentially methylated between baseline and follow-up samples. Models were fit to beta values (which represent the proportion methylated) for each CpG site separately. We compared results from two models. The first model adjusted

for PCs capturing >90% of the technical variability (batch effects) and a random intercept for each individual. The second model also included estimated cell type proportions (CD4+ T cells, CD8+ T cells, monocytes and neutrophils), Hispanic ethnicity and pack-year residuals in an effort to reduce confounding bias. Results are reported from the second, fully adjusted model. CpG sites associated with follow-up at a false discovery rate adjusted p value <0.05 (q value) are considered statistically significant.<sup>22</sup> As a sensitivity analysis, we ran the model again excluding the samples from the one female participant; effect estimates remained unchanged at the significant CpG sites (correlation coefficient=0.99). We also ran the model excluding the pack-year residuals since all participants are current non-smokers, and estimates for the significant CpG sites were unchanged.

We examined results at specific CpG sites that were identified as differentially methylated between new recruit and incumbent firefighters and/or were predictive of years in the service in our previous study<sup>14</sup>; 13 of the 16 CpG sites were available in our dataset. We also compared statistically significant CpG sites identified in this study to those previously associated with smoking<sup>10</sup> or air pollution<sup>23</sup> in adults.

We conducted a pathway analysis with the differentially methylated genes at follow-up. The CpG sites that changed over time according to the fully adjusted model (q<0.05) annotated to 408 unique genes included in the Ingenuity Knowledge Base of the Ingenuity Pathway Analysis (IPA) software (QIAGEN Inc, <https://www.qiagenbioinformatics.com/products/ingenuity-pathway-analysis>). IPA uses known relationships between transcriptional regulators and their target genes to test for significant enrichment in gene sets linked to functions and diseases.<sup>24</sup> We used the core analysis function and identified canonical pathways and disease gene sets enriched among our results, and considered pathways with a q value <0.05 to be statistically significant.

We examined associations between cumulative fire-hours and cumulative fire-runs for all fires and structure fires only with DNA methylation at the 680 CpG sites that changed over time. Fire-hours and fire-runs were natural log-transformed after adding one, and used as continuous variables in models. Models were adjusted for cell types, batch PCs, pack-years residual, ethnicity and length of service. The latter was included as a proxy for the cumulative impact of time in the fire service. Relationships between each fire-variable and DNA methylation were considered statistically significant at a q value <0.05. We ran the same models again including adjustment for the most recent exposure, approximated by days since most-recent fire-run (for all fires or structure-fires only; natural log-transformed) and compared results to assess the impact of chronic versus acute exposure.<sup>17</sup>

## RESULTS

We compared DNA methylation in blood leucocytes across repeat samples from 50 new recruits with an average of 26.5 (±SD 4.5) months between baseline and follow-up (table 1). Participants were non-smokers by design and primarily male (98%), white (94%) and non-Hispanic (88%). Proportion of monocytes was lower at follow-up (0.11±0.08 at baseline and 0.08±0.03 at follow-up, p value=0.005 for paired t-test for unequal variances). Participants accumulated a range of fire-hours with geometric means of 26.4 (range 8.2–53.6) and 13.2 (range 2.4–28.7) for all and structure fires, respectively. The geometric means (ranges) for fire-runs were 48.4 (22–100) for all fires and 16.3 (4–36) for structure fires.

**Table 1** Study population characteristics for 50 new recruit firefighters at baseline and follow-up

	n (%)	Mean (SD)
Male	49 (98)	
Female	1 (2)	
<i>Ethnicity</i>		
Hispanic	6 (12)	
Non-Hispanic	44 (88)	
<i>Race</i>		
White	47 (94)	
Black	3 (6)	
BMI (kg/m <sup>2</sup> ) at baseline		26.0 (2.9)
	<b>Baseline visit</b>	<b>Follow-up visit</b>
	<b>Mean (SD)</b>	<b>Mean (SD)</b>
Age (years)	28.0 (5.9)	30.2 (6.0)
Time in between visits (months)	–	26.5 (4.5)
<i>Fire exposure between baseline and follow-up*</i>		
Fire-hours	–	26.4 (0.4)
Fire-runs	–	48.4 (0.4)
Days since most recent fire	–	17.7 (1.8)
Fire-hours (structure only)	--	13.2 (0.5)
Fire-runs (structure only)	--	16.3 (0.5)
Days since most recent fire (structure only)	–	28.9 (2.4)
<i>Estimated cell type proportions (%)†</i>		
Neutrophils	0.55 (0.24)	0.58 (0.10)
CD4+ T cells	0.12 (0.07)	0.13 (0.05)
CD8+ T cells	0.11 (0.06)	0.11 (0.04)
Monocytes	0.11 (0.08)‡	0.08 (0.03)‡
B cells	0.06 (0.03)	0.06 (0.02)
Natural killer cells	0.06 (0.03)	0.06 (0.03)
<i>Estimated smoking§</i>		
Pack years	–20.4 (7.1)	0.8 (6.9)
Pack years residual	–21.7 (7.6)	–0.5 (7.3)

\*For the fire exposure variables, fire-hours indicates cumulative time at fires since follow-up; fire-runs indicates the cumulative number of fire-runs since follow-up; These are listed for all fire incident types as well as for structural-only. Geometric means and SD are listed as the distributions were skewed.

†Cell type proportions are estimated from DNA methylation data according to the established algorithm by Houseman *et al.*<sup>39</sup>

‡Differed across time points (p<0.05 for paired t-test for unequal variances).

§Lifetime smoking pack-years were estimated from the DNA methylation data using an algorithm by Lu *et al.*<sup>40</sup> All participants reported being non-smokers at time of the study, but this algorithm also estimates past exposure to smoking; values are relative and not absolute.

BMI, body mass index.

## Epigenome-wide approach comparing baseline to follow-up

In the main statistical model, 388 CpG sites had lower and 292 had greater methylation at follow-up (q<0.05; online supplemental table 1 shows all 680 CpG sites and table 2 shows the 60 sites with at least 5% methylation difference). Effect sizes and significance values were similar in the model without cell-type adjustment (not shown). The loci with at least 5% methylation change included two each in the genes *FTO*, *PHACTR1* and *PIK3R1*. At follow-up, DNA methylation was higher in a CpG site within the first exon of *FTO* and lower at a CpG site in an alternate promoter. The two sites with decreased methylation at follow-up in *PHACTR1* are in the second intron of the gene, and other CpG sites included on the array in the same region show a similar relationship. The significant loci in *PIK3R1* are in the promoter region of the gene. Genes with one statistically significant loci included non-coding RNA genes (*LINC01420* and

**Table 2** Significantly differentially methylated CpG sites when comparing baseline and follow-up samples from new recruits (with q value <0.05 and absolute difference >5%)

Probe ID	Genomic location*	Gene name	Estimate (SE)†	P value	q value
Decreased methylation at follow-up					
cg11835347	chr1: 113248232	<i>RHOC</i>	-0.054 (0.011)	1.09E-05	0.035
cg16265542	chr1: 152814831	<i>LCE6A</i>	-0.058 (0.012)	8.23E-06	0.032
cg21721331	chr1: 157670877	<i>FCRL3</i>	-0.061 (0.013)	2.13E-05	0.043
cg02928345	chr1: 224411698	<i>NA</i>	-0.065 (0.014)	8.08E-06	0.032
cg15591386	chr1: 76265299	<i>MSH4</i>	-0.054 (0.012)	2.67E-05	0.044
cg03740864	chr10: 120660492	<i>NA</i>	-0.054 (0.01)	8.46E-07	0.023
cg02884943	chr10: 72725905	<i>NA</i>	-0.059 (0.013)	1.71E-05	0.040
cg10967759	chr10: 73555025	<i>CDH23</i>	-0.071 (0.015)	7.81E-06	0.032
cg23024158	chr10: 78011952	<i>C10orf11</i>	-0.051 (0.011)	2.36E-05	0.043
cg03762984	chr11: 29355671	<i>NA</i>	-0.081 (0.016)	4.70E-06	0.027
cg01078446	chr12: 115113212	<i>TBX3</i>	-0.05 (0.01)	1.31E-05	0.037
cg18956104	chr12: 119621039	<i>HSPB8</i>	-0.059 (0.012)	3.68E-06	0.026
cg12248652	chr12: 132703589	<i>GALNT9</i>	-0.056 (0.011)	3.64E-06	0.026
cg02121135	chr14: 24858912	<i>NA</i>	-0.073 (0.015)	4.82E-06	0.027
cg02938807	chr14: 63785523	<i>GPHB5</i>	-0.069 (0.015)	2.72E-05	0.044
cg02428178	chr15: 49104237	<i>CEP152</i>	-0.053 (0.011)	9.69E-06	0.034
cg04245616	chr15: 59543693	<i>MYO1E</i>	-0.072 (0.017)	4.20E-05	0.048
cg06297541	chr16: 22384949	<i>CDR2</i>	-0.053 (0.011)	1.35E-05	0.037
cg12891543	chr16: 53958626	<i>FTO</i>	-0.052 (0.012)	3.09E-05	0.045
cg07280206	chr16: 56554249	<i>BBS2</i>	-0.063 (0.01)	1.61E-07	0.016
cg03432196	chr18: 9643805	<i>NA</i>	-0.063 (0.013)	6.43E-06	0.029
cg19995259	chr19: 53795827	<i>BIRC8</i>	-0.056 (0.013)	3.53E-05	0.046
cg16903817	chr2: 114655480	<i>ACTR3</i>	-0.09 (0.019)	7.62E-06	0.031
cg16262572	chr2: 122479703	<i>NIFK-AS1</i>	-0.052 (0.01)	2.53E-06	0.026
cg25296103	chr2: 145268533	<i>ZEB2</i>	-0.06 (0.012)	5.25E-06	0.028
cg00441550	chr20: 29955998	<i>DEFB118</i>	-0.06 (0.013)	2.21E-05	0.043
cg16145176	chr21: 25596030	<i>NA</i>	-0.06 (0.013)	2.32E-05	0.043
cg17885233	chr3: 132450221	<i>NPHP3-AS1</i>	-0.051 (0.011)	1.84E-05	0.041
cg13166622	chr3: 150904863	<i>MED12L</i>	-0.081 (0.016)	1.64E-06	0.025
cg03520471	chr3: 97753623	<i>GABRR3</i>	-0.054 (0.012)	2.30E-05	0.043
cg16350196	chr4: 137426420	<i>NA</i>	-0.052 (0.011)	2.36E-05	0.043
cg20300412	chr4: 65749341	<i>NA</i>	-0.064 (0.014)	3.07E-05	0.045
cg21359538	chr4: 76440740	<i>RCHY1</i>	-0.062 (0.014)	3.05E-05	0.045
cg03498271	chr5: 38427885	<i>EGFLAM</i>	-0.055 (0.012)	1.12E-05	0.036
cg06887251	chr5: 67576008	<i>PIK3R1</i>	-0.054 (0.012)	2.83E-05	0.045
cg10874300	chr5: 67588385	<i>PIK3R1</i>	-0.066 (0.011)	4.36E-08	0.014
cg04708601	chr6: 101880078	<i>GRIK2</i>	-0.051 (0.011)	2.19E-05	0.043
cg24105728	chr6: 13007033	<i>PHACTR1</i>	-0.054 (0.011)	6.61E-06	0.029
cg18742528	chr6: 13053520	<i>PHACTR1</i>	-0.055 (0.011)	5.83E-06	0.029
cg27509293	chr6: 14919597	<i>NA</i>	-0.057 (0.013)	3.36E-05	0.046
cg08188318	chr6: 34984953	<i>ANKS1A</i>	-0.093 (0.02)	1.24E-05	0.037
cg10420626	chr6: 43741154	<i>VEGFA</i>	-0.057 (0.013)	2.72E-05	0.044
cg00325383	chr6: 85404488	<i>LOC102724201</i>	-0.057 (0.012)	9.43E-06	0.034
cg19989663	chr7: 115981565	<i>NA</i>	-0.056 (0.013)	4.46E-05	0.050
cg03083251	chr7: 135408513	<i>SLC13A4</i>	-0.076 (0.016)	6.70E-06	0.029
cg12018852	chr7: 138777233	<i>ZC3HAV1</i>	-0.052 (0.01)	4.63E-06	0.027
cg05753918	chr7: 14899040	<i>NA</i>	-0.065 (0.013)	2.32E-06	0.026
cg04946588	chr7: 86271783	<i>GRM3</i>	-0.052 (0.011)	1.66E-05	0.040
cg21637741	chr8: 69834365	<i>LINC01592</i>	-0.052 (0.011)	2.40E-05	0.043
cg15728672	chr8: 89189971	<i>MMP16</i>	-0.059 (0.011)	1.64E-06	0.025
cg01761595	chr8: 9821723	<i>NA</i>	-0.069 (0.015)	1.70E-05	0.040
cg14611112	chr9: 139643351	<i>LCN6</i>	-0.053 (0.011)	6.49E-06	0.029
cg03779244	chrX: 56771607	<i>LINC01420</i>	-0.085 (0.016)	1.60E-06	0.025
Increased methylation at follow-up					

continued

Table 2 continued

Probe ID	Genomic location*	Gene name	Estimate (SE)†	P value	q value
cg19190900	chr2: 37553621	NA	0.053 (0.012)	2.23E-05	0.043
cg25229577	chr3: 58367583	PXK	0.062 (0.013)	6.81E-06	0.029
cg00367499	chr5: 170634447	RANBP17	0.062 (0.014)	3.81E-05	0.048
cg14396995	chr7: 42278089	GLI3	0.06 (0.013)	1.86E-05	0.041
cg21156439	chr9: 94716496	NA	0.051 (0.011)	1.57E-05	0.039
cg00625110	chr16: 53741731	FTO	0.069 (0.014)	3.35E-06	0.026
cg01154210	chr21: 27493310	APP	0.102 (0.022)	1.63E-05	0.039

NA means the CpG site is not within a gene or within a known feature (eg, promoter) of a specific gene.  
 \*Genomic location is according to genome build GRCh37/hg19.  
 †Effect estimates represent the proportion of methylation difference at follow-up compared with baseline, adjusted for batch, cell type estimates, Hispanic ethnicity, estimated smoking pack-years and a random intercept for individual to account for the repeated sampling design.

*LINC01592*), genes involved in neurological function (*GRIK2*, *APP*, *ACTR3*, *GABARR3*, *ANKS1A*, *GRM3*, *PXK*, *GLI3*), immune function (*GPHB5*, *DEPB118*, *ZC3H4V1*), and genes that have been linked to multiple cancers (*MM16*, *PIK3R1*, *RCHY1*, *ZEB2*, *CEP152*, *HSPB8*, *TBX3*, *FCLR3* and *RHOC*).

Loci identified as differentially methylated between new recruits and incumbents in our previous cross-sectional study were not among the CpG sites identified with  $q < 0.05$  in the present study.<sup>14</sup> Four had raw p values  $< 0.05$ , but the association was not always in the same direction as the previous results (online supplemental table 2). While results did not replicate, this study is comparing short-term changes among the same individuals while the previous study compared two separate groups of firefighters with 14 years difference in experience, on average.

In the pathway analysis of the 680 CpG sites with differential methylation, six canonical pathways were significantly enriched ( $q < 0.05$ ; table 3). In the disease and functions analysis, 123 annotations were enriched among the differentially methylated genes ( $q < 0.05$ , online supplemental table 3) within 27 disease categories—11 of which are directly cancer related (table 4). The rest of the enriched categories relate to cardiovascular disease, cell signalling and movement, and gene expression.

### Fire-exposures analysis

There were linear relationships, suggestive of dose–response, between fire variables and 140 of the 680 loci that changed over time ( $q < 0.05$ , online supplemental table 4). DNA methylation at 108 and 78 CpG sites were associated with fire-runs for all and structure fires, respectively (figure 1). For fire-hours, 27 CpG sites were associated with all fire-hours and one CpG site with structure fire-hours only. There were 22 CpG sites that were associated with at least three of the fireground exposure variables, including one within the promoter region of *IQCC* that was positively associated with all four. Among the 32 sites

only associated with structure fire-runs, 15 of them may reflect a unique association with structure fires since the q value was between 0.05 and 0.1 with all fire-runs or hours for the other 17 loci.

There was limited evidence for the associations being driven by acute versus cumulative exposure during the follow-up period. The effect estimates at the 680 CpG sites correlated strongly (correlation coefficients 0.92–0.99) when comparing results from the models with and without adjustment for acute exposure. Days since most recent fire was associated with one CpG site (probe ID cg26723045 in the gene *SCUBE2*; effect estimate (SE)  $-0.012$  (0.003),  $q = 0.046$ ) in the model with fire-hours. Days since most recent fire was not significantly associated with DNA methylation at any other loci.

### DISCUSSION

In this pilot study of new firefighters, we observed differences in DNA methylation at 680 CpG sites when comparing samples taken before any fireground exposures to matched samples collected after 20–37 months in the service, including 60 CpG sites that differed by at least 5%. These sites were enriched in pathways involved in cancers, neurological function, cell signalling, cell movement and transcriptional regulation. When assessing the relationship with proxies for cumulative fireground exposures, there were linear associations between fire-hours or fire-runs for all fires or structural fires only with 140 of these CpG sites, including several that were uniquely associated with structural fire-runs. These associations did not depend on time since most recent fire-run, and therefore may reflect cumulative exposures since joining the fire department. These results provide preliminary evidence for epigenetic mechanisms that may underlie multiple adverse health outcomes firefighters face after years in the service. Alternatively, differentially methylated loci could serve as biomarkers of cumulative firefighting

Table 3 Canonical pathways enriched among the genes differentially methylated between baseline and follow-up

Ingenuity canonical pathways*	Total genes in pathway (n)	q value for enrichment	Genes in pathway with less methylation at follow-up (n)	Genes in pathway with more methylation at follow-up (n)
Molecular mechanisms of cancer	437	0.0011	12	11
Colorectal cancer metastasis signalling	262	0.0011	11	6
ERBB signalling	93	0.0044	5	4
UVB-induced MAPK signalling	51	0.0044	3	4
Reelin signalling in neurons	125	0.0069	5	5
Production of nitric oxide and reactive oxygen species in macrophages	187	0.0098	6	6

\*These pathways were identified with IPA software (Qiagen). Pathways significantly enriched at a cut-off of  $q < 0.05$  are shown here.

**Table 4** Enriched gene sets annotated to disease and disease-related functions in IPA among differentially methylated genes comparing baseline to follow-up ( $q < 0.05$ )

Disease category	Enriched disease annotations (gene-sets) in this category (n)
Cancer, cell cycle, organismal injury and abnormalities	3
Cancer, dermatological diseases and conditions, organismal injury and abnormalities	1
Cancer, endocrine system disorders, gastrointestinal disease, organismal injury and abnormalities	5
Cancer, gastrointestinal disease, organismal injury and abnormalities	32
Cancer, gastrointestinal disease, organismal injury and abnormalities, tumour morphology	1
Cancer, haematological disease, immunological disease, organismal injury and abnormalities	3
Cancer, neurological disease, organismal injury and abnormalities	19
Cancer, organismal injury and abnormalities	23
Cancer, organismal injury and abnormalities, reproductive system disease	4
Cancer, organismal injury and abnormalities, respiratory disease	5
Cancer, organismal injury and abnormalities, tumour morphology	1
Cardiovascular disease, cardiovascular system development and function, organ morphology, organismal development, organismal injury and abnormalities, skeletal and muscular disorders	1
Cardiovascular system development and function, cellular development, cellular growth and proliferation	1
Cardiovascular system development and function, organ development, organ morphology	1
Cell cycle	3
Cell-to-cell signalling and interaction	1
Cell-to-cell signalling and interaction, haematological system development and function	1
Cellular development	1
Cellular development, cellular growth and proliferation, haematological system development and function, haematopoiesis, tissue development	1
Cellular movement	4
Cellular movement, nervous system development and function	1
Connective tissue disorders, inflammatory disease, inflammatory response, organismal injury and abnormalities, skeletal and muscular disorders	1
Dermatological diseases and conditions, organismal injury and abnormalities	1
Developmental disorder, hereditary disorder, neurological disease, organismal injury and abnormalities	1
Gene expression	6
Haematological system development and function, haematopoiesis	1
Neurological disease, organismal injury and abnormalities	1

\*These gene-sets were identified with IPA software (Qiagen). Summary is shown of enriched gene-sets that fall under broader categories of disease functions. For full list of statistically significant gene-sets, see online supplemental table 3.

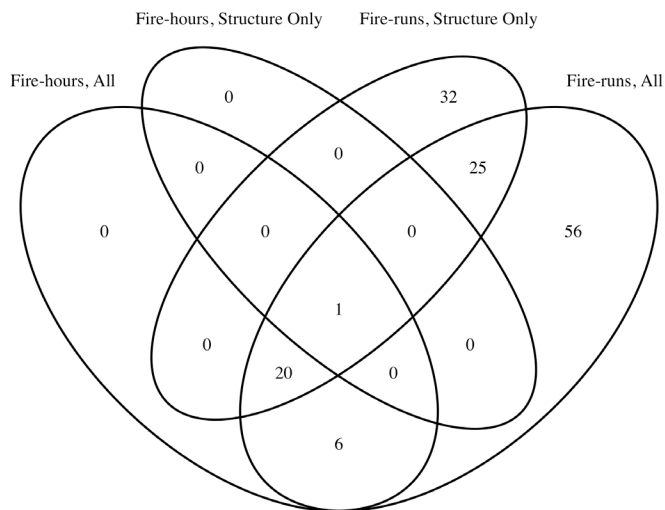
exposures. Further work is needed to determine which of the many exposures firefighters experience contribute to these associations.

This study builds on our previous research comparing new recruits to incumbents in a cross-sectional study<sup>14 16</sup> by comparing epigenetic data from matched samples pre-employment and postemployment in the fire service. In the previous study, microRNA expression and DNA methylation differed between new recruits and incumbents. However, since these were one-time collection of samples, the extent to which occupational exposures and hazards contributed to these differences is uncertain. The inception cohort design used in the current study enables us to infer whether differences between baseline and follow-up are attributed to occupational exposures. We recently reported miRNA differences in this same set of firefighters with longitudinal follow-ups and reported changes in multiple miRNAs associated with time to follow-up, as well as association of some miRNAs with measures of cumulative fireground exposure and most recent fire.<sup>17</sup> Overall, the miRNA study and the DNA methylation results reported here provide evidence that even a short time (~2–3 years) in the fire service may be associated with an altered epigenome. It is unlikely these loci changed because of impacts from short-term ageing during the time period as only one of the 680 loci are among loci known to

predict chronological age.<sup>25</sup> Furthermore, widespread changes by ageing tend to occur over decades instead of years.<sup>26 27</sup>

Our results could serve as biomarkers of exposure and may have implications for future disease risks. Firefighters have increased incidence and mortality for specific cancers, including those of the digestive tract, bladder, prostate, testicles, thyroid, brain and blood, among others.<sup>3 4 28 29</sup> Disease functions enriched among the differentially methylated genes included several types of gastrointestinal, brain and blood cancers (online supplemental table S3). Cardiac events are also a leading cause of death in firefighters,<sup>30</sup> consistent with the identification of enriched pathways involving cardiovascular disease. There is also evidence that firefighter exposures such as shift work could lead to neurocognitive decline,<sup>31</sup> consistent with the findings of the current study involving enriched gene pathways for neurological functions.

The associations between crude proxies of fireground exposure and DNA methylation suggest that exposure to products of combustion may be responsible. We previously measured increased concentration of PAH metabolites, proxies of combustion byproducts, in the urine of Tucson firefighters following fireground incidents.<sup>32</sup> PAH exposures have been associated with altered DNA methylation,<sup>33</sup> as have other chemicals such as formaldehyde<sup>34</sup> which are commonly measured at the fireground. Hypomethylation of the *DUSP22* promoter in a



**Figure 1** Overlap of CpG sites associated with proxies of fireground exposures. When comparing DNA methylation in blood leucocyte samples from new recruits with a repeat sample collected approximately 2 years later, 680 CpG sites had altered methylation in adjusted linear mixed models ( $q < 0.05$ ). We tested the association of cumulative fireground exposures from all fires and structure-fires only within this time period with DNA methylation at these 680 loci. 140 of them were associated with at least one exposure variable ( $q < 0.05$ ), with overlap indicated in the Venn diagram.

candidate gene study comparing firefighters to controls was previously reported, and treatment of cells with benzo-a-pyrene reduced methylation at the same gene demonstrating biological plausibility for PAH exposures as epigenetic modifiers.<sup>35</sup> In our study, DNA methylation at 11 out of 12 CpG sites included on the array near the transcription start site of *DUSP22* had decreased methylation at follow-up compared with baseline, yet results were not statistically significant.

We compared statistically significant results with those from epigenome-wide associations of cigarette smoking and air pollution exposure among adults to assess whether common signals emerged. A meta-analysis of nearly 16 000 adults from 16 cohorts with blood derived DNA methylation data from the Infinium 450K array identified 18 760 and 2623 CpG sites with differential methylation ( $q < 0.05$ ) when comparing current and former smokers to controls, respectively.<sup>10</sup> 305 of the 680 differentially methylated sites in our study were covered on the 450K array. Among these, 25 were reported as differentially methylated in current smokers compared with non-smokers including four that also differed in former smokers (online supplemental table S1).<sup>10</sup> A systematic review of epigenome-wide association studies focused on adult air pollution exposure compared results across eleven studies using the Infinium 450K or EPIC arrays, and reported 201 CpG sites that were associated with component(s) of air pollution.<sup>23</sup> None of the CpG sites reported here that changed in firefighters were among the air pollution-related sites. However, there was heterogeneity across studies in component of air pollution measured and duration of exposure, and the 201 CpG sites did not replicate across air pollution studies either. This comparison does not provide evidence for a

common epigenetic signature of smoke/combustion byproduct exposure in firefighters and the general population.

We hypothesised that structural fire exposures would have different associations than other types of fires. Structural fires are more likely to involve interior responses by firefighters, and interior responses are associated with increased levels of urinary PAH metabolites compared with exterior responses.<sup>32</sup> There were 15 CpG sites that were associated with fire-runs only for structural fires ( $q < 0.05$ ) with little evidence for an association with total fire runs or hours ( $q > 0.1$ ). The most notable genes represented among these sites were *MAPK9* which increases the stability of the tumour suppressor gene *TP53*,<sup>36</sup> and *PEAR1* which has been linked to endometrial, renal, and lung cancers.<sup>37</sup>

This study had several strengths. This is the first longitudinal analysis of DNA methylation in firefighters, with an inception cohort design. We enrolled non-smoking new recruits prior to any occupational exposure and compared epigenetic profiles after live-fire training. The repeat sampling design reduces confounding bias by a variety of demographic and non-occupational exposures. Our two-tiered analysis plan included an epigenome-wide approach, and then assessment of associations with proxies of fireground exposures. This approach has advantages but may have limited our ability to find all CpG sites associated with specific fireground exposures, given adjustment for multiple comparisons. Other limitations of this study include the sample size which limits ability to detect all true associations, especially those with small effect sizes. Given the design, it is possible that epigenetic changes reported here reflect ageing over the 2 years of follow-up instead of occupation. However, this is unlikely as the top CpG sites were not among those known to correlate with chronological age in adults.<sup>25</sup> Our fireground exposure metrics were not specific (ie, we did not measure exposure biomarkers of specific chemicals). The majority of study participants were male, white, non-Hispanic, and came from one location; thus sex, regional or race/ethnicity-specific associations could not be assessed. Our study lacked a non-firefighter control group with repeat measures of DNA methylation. Since we previously reported epigenetic differences by Hispanic ethnicity among firefighters,<sup>38</sup> epigenetic biomarkers should be profiled in a diverse cohort (eg, by geography, race, ethnicity and sex) in order to determine generalisability.

## CONCLUSION

In conclusion, this pilot study provides evidence consistent with previous research that molecular biomarkers including DNA methylation may change from the cumulative burden of exposures encountered when firefighting. This is important because DNA methylation could be used as a biomarker of exposures and could inform occupational health risk assessment for firefighters. The study findings merit further investigation as epigenetics alterations as associated with many diseases states and constitute one of the key characteristics by which carcinogens exert their effects.<sup>13</sup>

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**Contributors** JLB and JMG designed the concept for this study and obtained funding. JLB, SB, SL, JG and DW were instrumental in the acquisition of data for this

study. JMG conducted statistical analysis and drafted the manuscript with critical intellectual input from AMJ, MAF and JLB. JLB is the guarantor for the research described in this publication. All authors approve the final version of the manuscript and accept responsibility for the accuracy and integrity of reported results.

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**Competing interests** None declared.

**Patient consent for publication** Not applicable.

**Ethics approval** This study involves human participants and was approved by the University of Arizona Institutional Review Board (IRB approval No. 1509137073). Participants gave informed consent to participate in the study before taking part.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** Data are available upon reasonable request. Data requests will be reviewed by the study's Oversight and Planning Board to address firefighter concerns prior to determination of sharing de-identified data which may include de-identified epigenomic (DNA methylation) data. This study is not a clinical trial. Contact the corresponding author, JLB, with requests.

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**SUPPLEMENTAL MATERIAL for:**

Repeat Measures of DNA Methylation in an Inception Cohort of Firefighters

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## SUPPLEMENTAL TABLES

**Supplemental Table S1.** All Significantly Differentially Methylated CpG Sites when comparing baseline and follow-up samples from new recruits (q-value<0.05)

Probe ID	Genomic Location <sup>a</sup>	Gene Name	Estimate (SE) <sup>b</sup>	p-value	q-value	CpG site associated with smoking: current vs. never? <sup>c</sup>	CpG site associated with smoking: former vs. never? <sup>c</sup>	Near CpG Island? <sup>d</sup>	Annotation Relative to Nearest Gene <sup>e</sup>
cg13798302	chr4: 100870323	<i>LOC256880</i>	-0.014 (0.002)	1.62E-08	0.01	no	no	North Shore	within 1500 bp of TSS within gene body
cg10874300	chr5: 67588385	<i>PIK3R1</i>	-0.066 (0.011)	4.36E-08	0.01	not tested	not tested	South Shelf	
cg12668515	chr9: 113861165	NA	-0.044 (0.007)	7.36E-08	0.01	not tested	not tested	Open Sea	
cg16668826	chr17: 12448991	NA	0.027 (0.005)	8.93E-08	0.01	not tested	not tested	Open Sea	
cg17636707	chr10: 30970470	NA	0.015 (0.002)	1.09E-07	0.01	no	no	Open Sea	
cg18105361	chr5: 135536668	NA	-0.044 (0.007)	1.06E-07	0.01	no	no	Open Sea	
cg05423480	chr15: 65189594	NA	-0.031 (0.005)	1.65E-07	0.02	not tested	not tested	Open Sea	
cg07280206	chr16: 56554249	<i>BBS2</i>	-0.063 (0.01)	1.61E-07	0.02	no	no	South Shore	within 1500 bp of TSS
cg02923300	chrX: 68759322	NA	0.037 (0.006)	2.87E-07	0.02	no	no	South Shore	
cg04853543	chr17: 77974147	<i>TBC1D16</i>	0.032 (0.006)	2.61E-07	0.02	not tested	not tested	Open Sea	within gene body
cg16216305	chr3: 127842716	<i>RUVBL1</i>	-0.002 (0)	3.06E-07	0.02	no	no	in CpG Island	within 200 bp of TSS
cg27608911	chr3: 115341429	<i>GAP43</i>	0.026 (0.005)	2.48E-07	0.02	no	no	Open Sea	within 1500 bp of TSS within gene body
cg25945533	chr19: 40883570	<i>PLD3</i>	0.023 (0.004)	3.57E-07	0.02	not tested	not tested	North Shelf	within gene body
cg15010903	chr17: 76850256	<i>TIMP2</i>	-0.046 (0.008)	3.90E-07	0.02	no	no	North Shore	3'UTR
cg01152629	chr19: 4705838	<i>DPP9</i>	0.023 (0.004)	4.44E-07	0.02	not tested	not tested	Open Sea	within gene body
cg00156769	chr1: 183498596	<i>SMG7</i>	0.015 (0.003)	1.04E-06	0.02	not tested	not tested	Open Sea	within gene body
cg01092213	chr7: 48127925	<i>UPP1</i>	-0.035 (0.006)	5.99E-07	0.02	no	no	North Shore	within 1500 bp of TSS
cg01739831	chr16: 89922539	<i>SPIRE2</i>	0.029 (0.005)	9.26E-07	0.02	no	no	South Shore	within gene body

cg03740864	chr10: 120660492	NA	-0.054 (0.01)	8.46E-07	0.02	not tested	not tested	Open Sea	
cg03923285	chr16: 412168	NA	-0.046 (0.008)	9.40E-07	0.02	no	no	South Shore	
cg04497992	chr16: 616212	<i>NHLRC4</i>	-0.042 (0.008)	8.60E-07	0.02	no	no	South Shore	within 1500 bp of TSS
cg05463966	chr11: 67803951	<i>NDUFS8</i>	-0.037 (0.007)	1.06E-06	0.02	no	no	North Shelf	within gene body
cg05632631	chr16: 24099614	<i>PRKCB</i>	0.017 (0.003)	1.08E-06	0.02	no	no	Open Sea	within gene body
cg12784120	chr17: 41847254	<i>DUSP3</i>	0.022 (0.004)	5.08E-07	0.02	no	no	Open Sea	within gene body
cg16001875	chr3: 47019411	<i>CCDC12</i>	0.029 (0.005)	6.90E-07	0.02	not tested	not tested	North Shore	within 1500 bp of TSS
cg16353975	chr12: 88531040	<i>CEP290</i>	0.017 (0.003)	1.02E-06	0.02	not tested	not tested	Open Sea	within gene body
cg18676539	chr8: 144575488	<i>ZC3H3</i>	0.025 (0.005)	9.87E-07	0.02	not tested	not tested	Open Sea	within gene body
cg19721787	chr1: 32670695	<i>IQCC</i>	0.035 (0.007)	8.30E-07	0.02	yes	no	in CpG Island	within 1500 bp of TSS
cg19815791	chr17: 76343835	NA	0.027 (0.005)	1.00E-06	0.02	not tested	not tested	Open Sea	
cg21457856	chr3: 148367697	NA	-0.022 (0.004)	1.13E-06	0.02	no	no	Open Sea	
cg22216159	chr3: 109746788	NA	-0.046 (0.009)	1.05E-06	0.02	not tested	not tested	Open Sea	
cg22385591	chr13: 72778607	NA	-0.036 (0.007)	1.14E-06	0.02	not tested	not tested	Open Sea	
cg23477670	chr8: 27114746	<i>STMN4</i>	-0.045 (0.008)	9.73E-07	0.02	not tested	not tested	Open Sea	5'UTR within gene body
cg23532197	chr10: 11908666	<i>C10orf47</i>	-0.033 (0.006)	8.80E-07	0.02	no	no	North Shelf	
cg23865100	chr3: 184344968	NA	-0.044 (0.008)	6.20E-07	0.02	not tested	not tested	Open Sea	
cg24067133	chr11: 79613887	NA	-0.046 (0.009)	7.29E-07	0.02	not tested	not tested	Open Sea	
cg25529557	chr6: 112145775	<i>FYN</i>	-0.044 (0.008)	1.07E-06	0.02	not tested	not tested	Open Sea	5'UTR within gene body
cg25983854	chr22: 47257568	<i>TBC1D22A</i>	0.018 (0.003)	1.03E-06	0.02	no	no	South Shore	within gene body
cg02359589	chr17: 8045663	<i>PER1</i>	0.03 (0.006)	1.19E-06	0.02	no	no	Open Sea	within gene body
cg13783035	chr22: 46154632	<i>ATXN10</i>	0.009 (0.002)	1.22E-06	0.02	not tested	not tested	Open Sea	within gene body
cg12369388	chr2: 47094435	NA	0.02 (0.004)	1.33E-06	0.02	not tested	not tested	Open Sea	
cg15086037	chr2: 40823629	NA	0.012 (0.002)	1.31E-06	0.02	not tested	not tested	Open Sea	
cg00555389	chr2: 178261381	<i>AGPS</i>	-0.04 (0.008)	1.42E-06	0.03	not tested	not tested	South Shelf	within gene body
cg02029108	chr7: 98609251	<i>TRRAP</i>	0.026 (0.005)	1.65E-06	0.03	not tested	not tested	South Shore	within gene body
cg02708501	chr17: 4350829	<i>SPNS3</i>	0.016 (0.003)	1.50E-06	0.03	not tested	not tested	Open Sea	within gene body
cg03779244	chrX: 56771607	<i>LINC01420</i>	-0.085 (0.016)	1.60E-06	0.03	not tested	not tested	Open Sea	within gene body

cg09417137	chr3: 9811912	<i>CAMK1</i>	-0.035 (0.007)	1.65E-06	0.03	not tested	not tested	South Shore	within 1500 bp of TSS
cg13166622	chr3: 150904863	<i>MED12L</i>	-0.081 (0.016)	1.64E-06	0.03	not tested	not tested	Open Sea	within gene body
cg15728672	chr8: 89189971	<i>MMP16</i>	-0.059 (0.011)	1.64E-06	0.03	not tested	not tested	Open Sea	within gene body
cg17214079	chr17: 37719431	NA	0.015 (0.003)	1.62E-06	0.03	not tested	not tested	Open Sea	
cg10992198	chr19: 36552038	<i>WDR62</i>	0.03 (0.006)	1.72E-06	0.03	not tested	not tested	Open Sea	within gene body
cg00137860	chr22: 26249504	<i>MYO18B</i>	-0.04 (0.008)	1.77E-06	0.03	not tested	not tested	Open Sea	within gene body
cg10764756	chr11: 126337070	<i>KIRREL3</i>	0.031 (0.006)	1.82E-06	0.03	not tested	not tested	Open Sea in CpG Island	within gene body
cg16688112	chr16: 88922774	<i>GALNS</i>	-0.029 (0.006)	1.82E-06	0.03	yes	no	Open Sea in CpG Island	within gene body
cg00625110	chr16: 53741731	<i>FTO</i>	0.069 (0.014)	3.35E-06	0.03	no	no	South Shelf	within gene body
cg00949337	chr20: 61181680	NA	0.022 (0.004)	2.65E-06	0.03	not tested	not tested	South Shelf	
cg01622399	chr11: 134387905	NA	-0.04 (0.008)	3.55E-06	0.03	not tested	not tested	Open Sea in CpG Island	
cg01862160	chr9: 135456402	NA	-0.035 (0.007)	3.25E-06	0.03	no	no	Open Sea in CpG Island	
cg02098857	chr17: 27441752	<i>MYO18A</i>	0.028 (0.005)	1.99E-06	0.03	not tested	not tested	Open Sea	within gene body
cg02319637	chrX: 68525486	NA	-0.046 (0.009)	2.43E-06	0.03	not tested	not tested	North Shore	
cg02996608	chr1: 23256885	NA	-0.027 (0.005)	3.05E-06	0.03	not tested	not tested	Open Sea	
cg03776062	chr17: 76390494	<i>PGS1</i>	0.009 (0.002)	3.68E-06	0.03	not tested	not tested	Open Sea	within gene body
cg03897241	chr7: 1808115	NA	0.013 (0.003)	2.03E-06	0.03	no	no	North Shore	
cg04639736	chr4: 142481583	NA	-0.034 (0.007)	2.81E-06	0.03	not tested	not tested	Open Sea	
cg04694057	chr12: 49763589	<i>SPATS2</i>	-0.041 (0.008)	3.35E-06	0.03	not tested	not tested	South Shelf	5'UTR
cg04974344	chr4: 132420800	NA	-0.04 (0.008)	2.64E-06	0.03	not tested	not tested	Open Sea	
cg05419854	chr17: 19398395	NA	0.023 (0.005)	3.38E-06	0.03	no	no	Open Sea	
cg05541640	chr3: 52008740	<i>ABHD14B</i>	-0.036 (0.007)	3.33E-06	0.03	yes	no	North Shore	within 200 bp of TSS
cg05753918	chr7: 14899040	NA	-0.065 (0.013)	2.32E-06	0.03	not tested	not tested	Open Sea	
cg06044060	chr9: 135880142	NA	-0.029 (0.006)	3.30E-06	0.03	not tested	not tested	Open Sea	
cg06492744	chr11: 65406254	<i>SIPA1</i>	-0.005 (0.001)	3.72E-06	0.03	no	no	North Shelf	5'UTR
cg07499197	chr19: 47921090	<i>MEIS3</i>	-0.032 (0.006)	2.80E-06	0.03	not tested	not tested	North Shore	within gene body
cg07664312	chr12: 18433550	<i>PIK3C2G</i>	0.019 (0.004)	3.48E-06	0.03	no	no	Open Sea	5'UTR
cg08448786	chr10: 82258519	<i>TSPAN14</i>	-0.035 (0.007)	3.77E-06	0.03	not tested	not tested	Open Sea	within gene body
cg08766380	chr17: 31107923	<i>MYO1D</i>	-0.039 (0.008)	3.80E-06	0.03	not tested	not tested	Open Sea	within gene body

cg09951898	chr4: 104022073	<i>BDH2</i>	0.015 (0.003)	3.02E-06	0.03	not tested	not tested	Open Sea	within 1500 bp of TSS
cg10353689	chr2: 70792316	NA	0.019 (0.004)	2.34E-06	0.03	not tested	not tested	Open Sea	
cg10778736	chr15: 45406362	<i>DUOX2</i>	-0.029 (0.006)	2.90E-06	0.03	no	no	North Shore	within 200 bp of TSS
cg11764115	chr19: 11660189	<i>CNN1</i>	0.024 (0.005)	2.03E-06	0.03	no	no	North Shore	within gene body
cg11796181	chr5: 142422241	<i>ARHGAP26</i>	0.013 (0.003)	3.11E-06	0.03	no	no	Open Sea	within gene body
cg11985186	chr1: 54964993	NA	-0.031 (0.006)	2.91E-06	0.03	not tested	not tested	North Shore	
cg12248652	chr12: 132703589	<i>GALNT9</i>	-0.056 (0.011)	3.64E-06	0.03	no	no	Open Sea	within gene body
cg12384419	chr2: 202685659	<i>CDK15</i>	-0.021 (0.004)	1.98E-06	0.03	not tested	not tested	Open Sea	within gene body
cg12709085	chr19: 35502231	<i>GRAMD1A</i>	-0.035 (0.007)	2.86E-06	0.03	not tested	not tested	Open Sea	within gene body
cg13092901	chr22: 50965373	<i>TYMP</i>	-0.032 (0.006)	2.89E-06	0.03	yes	yes	Open Sea	in CpG Island
cg14412992	chr5: 125706935	<i>GRAMD3</i>	0.033 (0.007)	3.47E-06	0.03	not tested	not tested	Open Sea	within gene body
cg14705319	chr5: 176938148	<i>DOK3</i>	-0.038 (0.008)	3.26E-06	0.03	no	no	Open Sea	within 1500 bp of TSS
cg15155209	chr3: 14502277	<i>SLC6A6</i>	0.022 (0.004)	3.14E-06	0.03	no	no	Open Sea	within gene body
cg15168816	chr6: 17282533	<i>RBM24</i>	-0.031 (0.006)	3.83E-06	0.03	no	no	South Shore	within 1500 bp of TSS
cg15281614	chr1: 160345932	NA	-0.042 (0.008)	2.76E-06	0.03	not tested	not tested	Open Sea	
cg15734764	chr10: 134266555	NA	-0.029 (0.006)	2.25E-06	0.03	no	no	North Shore	
cg16262572	chr2: 122479703	<i>NIFK-AS1</i>	-0.052 (0.01)	2.53E-06	0.03	not tested	not tested	Open Sea	within gene body
cg17353568	chr10: 76661092	<i>KAT6B</i>	-0.043 (0.009)	3.33E-06	0.03	not tested	not tested	Open Sea	within gene body
cg17410093	chr2: 232650620	<i>COPS7B</i>	0.023 (0.005)	1.90E-06	0.03	not tested	not tested	North Shore	within 1500 bp of TSS
cg17777792	chr1: 226285808	NA	-0.036 (0.007)	3.05E-06	0.03	not tested	not tested	Open Sea	
cg18032827	chr1: 185227307	<i>SWT1</i>	0.027 (0.005)	3.34E-06	0.03	not tested	not tested	Open Sea	within gene body
cg18164926	chr11: 62600230	<i>STX5</i>	-0.041 (0.008)	2.23E-06	0.03	not tested	not tested	South Shore	within 1500 bp of TSS
cg18661379	chr10: 104393081	<i>SUFU</i>	-0.029 (0.006)	2.89E-06	0.03	no	no	Open Sea	3'UTR
cg18956104	chr12: 119621039	<i>HSPB8</i>	-0.059 (0.012)	3.68E-06	0.03	not tested	not tested	Open Sea	within gene body
cg19465330	chr11: 61084101	<i>DDB1</i>	0.023 (0.005)	3.81E-06	0.03	not tested	not tested	Open Sea	within gene body

cg19842279	chr17: 39554246	<i>KRT31</i>	-0.024 (0.005)	3.69E-06	0.03	not tested	not tested	Open Sea	within 1500 bp of TSS
cg19882915	chr8: 102451058	NA	0.024 (0.005)	3.44E-06	0.03	no	no	Open Sea	
cg21146224	chr9: 13492139	NA	-0.032 (0.006)	3.06E-06	0.03	not tested	not tested	Open Sea	
cg21289437	chr13: 112692270	NA	0.025 (0.005)	3.55E-06	0.03	no	no	South Shore	
cg21611056	chr20: 3776172	<i>CDC25B</i>	-0.038 (0.007)	2.73E-06	0.03	not tested	not tested	North Shore	within 1500 bp of TSS
cg21723874	chr19: 51531123	<i>KLK11</i>	0.036 (0.007)	2.84E-06	0.03	not tested	not tested	Open Sea	5'UTR
cg22071573	chr19: 8506975	NA	0.026 (0.005)	2.99E-06	0.03	not tested	not tested	North Shelf	
cg24144259	chr5: 88875631	NA	-0.042 (0.008)	3.65E-06	0.03	not tested	not tested	Open Sea	
cg24924295	chr17: 999104	<i>ABR</i>	-0.029 (0.006)	3.54E-06	0.03	not tested	not tested	Open Sea	within gene body
cg26128821	chr19: 19511134	<i>GATAD2A</i>	0.026 (0.005)	2.83E-06	0.03	not tested	not tested	Open Sea	5'UTR
cg26859666	chr1: 167883298	<i>ADCY10</i>	0.011 (0.002)	3.29E-06	0.03	no	no	Open Sea in CpG Island	within 1st exon
cg27380788	chr16: 4526765	<i>HMOX2</i>	0.003 (0.001)	3.85E-06	0.03	no	no	Open Sea	5'UTR
cg27639525	chr1: 25029378	NA	0.021 (0.004)	2.89E-06	0.03	not tested	not tested	Open Sea in CpG Island	
cg00187535	chr19: 7747028	<i>TRAPPC5</i>	-0.038 (0.008)	3.92E-06	0.03	no	no	Open Sea	5'UTR
cg25502462	chrX: 48620142	<i>GLOD5</i>	0.027 (0.005)	4.03E-06	0.03	no	no	Open Sea	within 200 bp of TSS
cg07241925	chr4: 1294566	<i>MAEA</i>	-0.029 (0.006)	4.07E-06	0.03	no	no	Open Sea	within gene body
cg03914662	chr11: 65910130	<i>PACS1</i>	-0.035 (0.007)	4.23E-06	0.03	not tested	not tested	Open Sea	within gene body
cg07589116	chr11: 123450089	<i>GRAMD1B</i>	0.024 (0.005)	4.21E-06	0.03	not tested	not tested	South Shore	within gene body
cg13087441	chr1: 3277000	<i>PRDM16</i>	0.027 (0.006)	4.22E-06	0.03	no	no	South Shore	within gene body
cg24851859	chr5: 27532684	NA	-0.047 (0.009)	4.14E-06	0.03	yes	no	Open Sea	
cg06230410	chr19: 19457887	<i>MAU2</i>	0.016 (0.003)	4.33E-06	0.03	not tested	not tested	Open Sea	within gene body
cg12354960	chr1: 156816460	<i>NTRK1</i>	0.02 (0.004)	4.34E-06	0.03	not tested	not tested	South Shore	within gene body
cg18062128	chr2: 97501603	NA	0.02 (0.004)	4.35E-06	0.03	no	no	North Shelf	
cg10015051	chr16: 65102943	<i>CDH11</i>	0.019 (0.004)	4.50E-06	0.03	no	no	Open Sea	5'UTR
cg11360415	chr17: 1059336	<i>ABR</i>	0.022 (0.005)	4.61E-06	0.03	not tested	not tested	Open Sea	within gene body
cg11835575	chr1: 3447205	<i>MEGF6</i>	-0.03 (0.006)	4.59E-06	0.03	not tested	not tested	North Shore	within gene body
cg12018852	chr7: 138777233	<i>ZC3HAV1</i>	-0.052 (0.01)	4.63E-06	0.03	not tested	not tested	Open Sea	within gene body

cg16327381	chr3: 119498036	<i>NR1I2</i>	0.031 (0.006)	4.63E-06	0.03	no	no	Open Sea	within 1500 bp of TSS
cg23222095	chr12: 27934956	<i>KLHL42</i>	0.012 (0.003)	4.51E-06	0.03	not tested	not tested	South Shore	within gene body
cg24418298	chr7: 2752273	<i>AMZ1</i>	0.024 (0.005)	4.61E-06	0.03	no	no	Open Sea	within gene body
cg27423238	chr16: 1420171	<i>UNKL</i>	0.024 (0.005)	4.51E-06	0.03	no	no	in CpG Island	within gene body
cg03762984	chr11: 29355671	NA	-0.081 (0.016)	4.70E-06	0.03	not tested	not tested	Open Sea	
cg03922340	chr3: 49397232	<i>GPX1</i>	-0.035 (0.007)	4.70E-06	0.03	not tested	not tested	South Shore	within 1500 bp of TSS
cg02121135	chr14: 24858912	NA	-0.073 (0.015)	4.82E-06	0.03	not tested	not tested	Open Sea	
cg02984966	chr18: 21266734	NA	-0.032 (0.007)	4.89E-06	0.03	no	no	North Shelf	
cg13212159	chr17: 38075554	<i>GSDMB</i>	0.022 (0.004)	4.90E-06	0.03	no	no	Open Sea	within 1500 bp of TSS
cg06692153	chr22: 38137445	<i>TRIOBP</i>	-0.028 (0.006)	4.95E-06	0.03	not tested	not tested	Open Sea	within gene body
cg11339587	chr19: 30298341	NA	0.024 (0.005)	5.02E-06	0.03	no	no	North Shelf	
cg15468600	chr7: 101633200	<i>CUX1</i>	0.026 (0.005)	5.04E-06	0.03	not tested	not tested	Open Sea	within gene body
cg03197505	chr19: 17597999	<i>SLC27A1</i>	0.022 (0.004)	5.08E-06	0.03	no	no	in CpG Island	within gene body
cg09044656	chr12: 130184851	<i>TMEM132D</i>	0.03 (0.006)	5.26E-06	0.03	no	no	in CpG Island	within gene body
cg16416987	chr1: 155177561	<i>THBS3</i>	-0.033 (0.007)	5.18E-06	0.03	no	no	North Shore	within gene body
cg21368996	chr2: 201593511	<i>AOX2P</i>	-0.029 (0.006)	5.26E-06	0.03	not tested	not tested	Open Sea	within gene body
cg25296103	chr2: 145268533	<i>ZEB2</i>	-0.06 (0.012)	5.25E-06	0.03	no	no	Open Sea	within gene body
cg16802508	chr11: 67070738	<i>SSH3</i>	-0.032 (0.006)	5.36E-06	0.03	no	no	North Shore	within 200 bp of TSS
cg03541759	chr5: 72794079	<i>BTF3</i>	-0.004 (0.001)	5.41E-06	0.03	no	no	in CpG Island	within 200 bp of TSS
cg07488549	chr10: 106052976	<i>GSTO2</i>	-0.042 (0.008)	5.52E-06	0.03	not tested	not tested	Open Sea	within gene body
cg17654217	chr7: 100282651	<i>GIGYF1</i>	0.021 (0.004)	5.50E-06	0.03	no	no	North Shelf	within gene body
cg16238149	chr13: 111173329	NA	-0.031 (0.006)	5.62E-06	0.03	no	no	Open Sea	
cg03933550	chr18: 55906325	<i>NEDD4L</i>	-0.048 (0.01)	5.78E-06	0.03	not tested	not tested	Open Sea	within gene body
cg07872794	chr5: 117897957	<i>HRAT56</i>	0.015 (0.003)	5.90E-06	0.03	not tested	not tested	Open Sea	within 200 bp of TSS
cg11887996	chr12: 120559003	NA	-0.027 (0.006)	5.85E-06	0.03	no	no	South Shelf	

cg13170967	chr5: 38695390	<i>OSMR-AS1</i>	-0.036 (0.007)	5.84E-06	0.03	not tested	not tested	Open Sea	within gene body
cg13304430	chr9: 139414185	<i>MIR4673</i>	0.01 (0.002)	5.88E-06	0.03	not tested	not tested	South Shore	within 200 bp of TSS
cg18742528	chr6: 13053520	<i>PHACTR1</i>	-0.055 (0.011)	5.83E-06	0.03	not tested	not tested	Open Sea	within gene body
cg00841090	chr17: 2651101	NA	-0.027 (0.006)	5.98E-06	0.03	no	no	North Shore	
cg06551987	chr21: 28563103	NA	0.018 (0.004)	6.01E-06	0.03	not tested	not tested	Open Sea in CpG Island	
cg02956806	chr9: 140174741	<i>C9orf167</i>	0.031 (0.006)	6.13E-06	0.03	no	no	Open Sea	3'UTR within gene body
cg03083251	chr7: 135408513	<i>SLC13A4</i>	-0.076 (0.016)	6.70E-06	0.03	not tested	not tested	Open Sea	
cg03432196	chr18: 9643805	NA	-0.063 (0.013)	6.43E-06	0.03	not tested	not tested	Open Sea	
cg04483304	chr15: 68933603	<i>CORO2B</i>	0.021 (0.004)	6.61E-06	0.03	not tested	not tested	Open Sea	5'UTR within gene body
cg04571417	chr16: 11224056	<i>CLEC16A</i>	0.021 (0.004)	6.73E-06	0.03	not tested	not tested	Open Sea	body
cg06016751	chr12: 6442329	<i>TNFRSF1A</i>	-0.034 (0.007)	6.53E-06	0.03	not tested	not tested	South Shelf	ExonBnd within gene body
cg06285037	chr7: 131233012	<i>PODXL</i>	0.021 (0.004)	6.53E-06	0.03	not tested	not tested	Open Sea in CpG Island	
cg10884953	chr19: 2579745	<i>GNG7</i>	-0.031 (0.006)	6.65E-06	0.03	no	no	Open Sea	5'UTR
cg11362074	chr19: 2706834	NA	-0.035 (0.007)	6.82E-06	0.03	no	no	South Shelf	
cg14611112	chr9: 139643351	<i>LCN6</i>	-0.053 (0.011)	6.49E-06	0.03	no	no	South Shelf	within 1500 bp of TSS
cg14678981	chr16: 57662244	<i>ADGRG1</i>	-0.026 (0.005)	6.81E-06	0.03	not tested	not tested	Open Sea	within 1st exon
cg15105253	chr14: 100063248	<i>CCDC85C</i>	0.014 (0.003)	6.66E-06	0.03	not tested	not tested	Open Sea in CpG Island	within gene body
cg15198739	chr22: 26908541	<i>TFIP11</i>	-0.003 (0.001)	6.32E-06	0.03	no	no	Open Sea	within 200 bp of TSS
cg15300024	chr2: 113487167	NA	-0.029 (0.006)	6.53E-06	0.03	not tested	not tested	Open Sea	
cg20253556	chr10: 30712431	NA	-0.028 (0.006)	6.43E-06	0.03	not tested	not tested	Open Sea	
cg21346966	chr2: 238341793	NA	-0.022 (0.005)	6.15E-06	0.03	no	no	Open Sea	
cg24105728	chr6: 13007033	<i>PHACTR1</i>	-0.054 (0.011)	6.61E-06	0.03	not tested	not tested	Open Sea	within gene body
cg24668049	chr16: 88614791	NA	-0.036 (0.007)	6.32E-06	0.03	not tested	not tested	Open Sea	
cg25229577	chr3: 58367583	<i>PXK</i>	0.062 (0.013)	6.81E-06	0.03	not tested	not tested	Open Sea	5'UTR within 200 bp of TSS
cg26833538	chr11: 67777715	<i>ALDH3B1</i>	-0.03 (0.006)	6.29E-06	0.03	yes	no	Open Sea	
cg05166976	chr2: 242842459	NA	0.022 (0.005)	6.95E-06	0.03	no	no	North Shore	
cg16054275	chr1: 169556022	<i>F5</i>	-0.038 (0.008)	6.91E-06	0.03	no	no	Open Sea	within 1500 bp of TSS
cg19677181	chr5: 153211415	NA	-0.042 (0.009)	6.91E-06	0.03	not tested	not tested	Open Sea	
cg16594092	chr5: 169911303	<i>KCNIP1</i>	-0.028 (0.006)	7.09E-06	0.03	not tested	not tested	Open Sea	within gene body



cg21455534	chr6: 170101504 chr13: 110124427	<i>C6orf120</i>	0.009 (0.002)	7.11E-06	0.03	no	no	North Shore	within 1500 bp of TSS
cg01387115		NA	-0.024 (0.005)	7.23E-06	0.03	not tested	not tested	Open Sea	
cg13418283	chr20: 61439240 chr12: 131273144	<i>OGFR</i>	0.025 (0.005)	7.32E-06	0.03	not tested	not tested	North Shelf	within gene body
cg05410283		NA	0.014 (0.003)	7.52E-06	0.03	no	no	Open Sea	
cg16903817	chr2: 114655480	<i>ACTR3</i>	-0.09 (0.019)	7.62E-06	0.03	not tested	not tested	Open Sea	5'UTR
cg10967759	chr10: 73555025	<i>CDH23</i>	-0.071 (0.015)	7.81E-06	0.03	not tested	not tested	Open Sea	within 1500 bp of TSS
cg23926670	chr12: 28121938	<i>PTHLH</i>	0.044 (0.009)	7.77E-06	0.03	no	no	North Shore	within gene body
cg10175261	chr20: 56419097	NA	0.02 (0.004)	7.90E-06	0.03	not tested	not tested	Open Sea	
cg02928345	chr1: 224411698	NA	-0.065 (0.014)	8.08E-06	0.03	no	no	Open Sea	
cg06753606	chr17: 40337708	<i>HCRT</i>	0.021 (0.004)	8.02E-06	0.03	not tested	not tested	South Shore	within 1500 bp of TSS
cg18066598	chr8: 64992450	NA	-0.046 (0.009)	8.05E-06	0.03	no	no	Open Sea	
cg16265542	chr1: 152814831 chr10: 108337483	<i>LCE6A</i>	-0.058 (0.012)	8.23E-06	0.03	no	no	Open Sea	within 1500 bp of TSS
cg26914953		<i>SORCS1</i>	-0.031 (0.006)	8.21E-06	0.03	not tested	not tested	Open Sea	within gene body
cg00599564	chr6: 29943209	<i>HCG9</i>	-0.025 (0.005)	8.35E-06	0.03	no	no	North Shore	within gene body
cg07551022	chr1: 205760086	<i>SLC41A1</i>	0.01 (0.002)	8.52E-06	0.03	no	no	Open Sea	3'UTR
cg18667648	chr11: 6626577	<i>ILK</i>	-0.034 (0.007)	8.35E-06	0.03	not tested	not tested	South Shore	5'UTR
cg21857190	chr2: 217913299	NA	-0.019 (0.004)	8.53E-06	0.03	no	no	Open Sea	
cg22867941	chr4: 1225044	<i>CTBP1</i>	0.032 (0.007)	8.50E-06	0.03	not tested	not tested	South Shore in CpG Island	within gene body
cg23098305	chr1: 228112951	<i>WNT9A</i>	0.034 (0.007)	8.37E-06	0.03	no	no		within gene body
cg25303556	chr22: 39348639	NA	-0.034 (0.007)	8.46E-06	0.03	not tested	not tested	Open Sea	
cg03515346	chr4: 1645766	<i>FAM53A</i>	0.016 (0.003)	8.82E-06	0.03	not tested	not tested	North Shore	within gene body
cg08295857	chr16: 88096588	<i>BANP</i>	0.032 (0.007)	9.00E-06	0.03	no	no	Open Sea	within gene body
cg13387425	chr12: 54402050	<i>HOXC8</i>	-0.032 (0.007)	8.99E-06	0.03	not tested	not tested	North Shore	within 1500 bp of TSS
cg14099540	chr9: 136018794	<i>RALGDS</i>	-0.032 (0.007)	9.00E-06	0.03	no	no	North Shore	within gene body
cg22306344	chr3: 49966773	<i>MON1A</i>	0.01 (0.002)	9.02E-06	0.03	no	no	North Shore	within gene body
cg11138095	chr13: 49794053	<i>MLNR</i>	-0.033 (0.007)	9.08E-06	0.03	no	no	North Shore	within 1500 bp of TSS

cg25181302	chr17: 74570181	<i>ST6GALNAC2</i>	0.02 (0.004)	9.19E-06	0.03	not tested	not tested	Open Sea	within gene body
cg00325383	chr6: 85404488	<i>LOC102724201</i>	-0.057 (0.012)	9.43E-06	0.03	not tested	not tested	Open Sea	within gene body
cg11073382	chr4: 120898808	NA	-0.04 (0.008)	9.47E-06	0.03	no	no	Open Sea	
cg11644454	chr1: 172417035	<i>C1orf105</i>	-0.036 (0.007)	9.45E-06	0.03	not tested	not tested	South Shelf	within gene body
cg18411043	chr1: 31221135	<i>LAPTM5</i>	-0.024 (0.005)	9.36E-06	0.03	no	no	Open Sea	within gene body
cg20118823	chr19: 1612208	<i>TCF3</i>	0.025 (0.005)	9.33E-06	0.03	no	no	North Shelf	within gene body
cg02383650	chr11: 3050362	<i>CARS</i>	0.019 (0.004)	9.61E-06	0.03	not tested	not tested	Open Sea	within gene body
cg02428178	chr15: 49104237	<i>CEP152</i>	-0.053 (0.011)	9.69E-06	0.03	no	no	South Shore	within 1500 bp of TSS
cg04255090	chr16: 85343936	NA	-0.03 (0.006)	9.72E-06	0.03	not tested	not tested	Open Sea	
cg11175192	chr2: 219724918	<i>WNT6</i>	-0.034 (0.007)	9.57E-06	0.03	no	no	in CpG Island	within gene body
cg17357892	chr21: 44914774	NA	-0.036 (0.008)	9.72E-06	0.03	not tested	not tested	Open Sea	
cg24935208	chr3: 89097455	NA	-0.031 (0.007)	9.77E-06	0.03	no	no	Open Sea	
cg10702418	chr7: 157090031	NA	-0.049 (0.01)	9.91E-06	0.03	no	no	North Shelf	
cg12587260	chr14: 73703163	<i>PAPLN</i>	-0.038 (0.008)	9.87E-06	0.03	not tested	not tested	North Shore	within 1500 bp of TSS
cg13979872	chr19: 44327981	NA	0.017 (0.004)	9.85E-06	0.03	no	no	South Shelf	
cg12202498	chr3: 15482605	<i>EAF1</i>	-0.026 (0.005)	9.97E-06	0.03	not tested	not tested	Open Sea	3'UTR
cg21907521	chr19: 49255510	<i>FUT1</i>	-0.029 (0.006)	1.01E-05	0.03	not tested	not tested	South Shore	5'UTR
cg25579675	chr14: 23846906	<i>CMTM5</i>	-0.03 (0.006)	1.03E-05	0.03	no	no	Open Sea	within gene body
cg07100050	chr10: 21390114	<i>NEBL</i>	-0.047 (0.01)	1.04E-05	0.03	not tested	not tested	Open Sea	within gene body
cg08141463	chr3: 119310381	NA	0.013 (0.003)	1.07E-05	0.03	no	no	Open Sea	
cg11369971	chr12: 15337635	<i>REERG</i>	-0.035 (0.007)	1.07E-05	0.03	not tested	not tested	Open Sea	within gene body
cg13766864	chr11: 74172851	<i>KCNE3</i>	-0.048 (0.01)	1.05E-05	0.03	no	no	Open Sea	5'UTR
cg16551513	chr8: 134261857	<i>NDRG1</i>	-0.043 (0.009)	1.07E-05	0.03	not tested	not tested	Open Sea	within gene body
cg22599985	chr12: 51420538	<i>SLC11A2</i>	-0.027 (0.006)	1.06E-05	0.03	not tested	not tested	South Shore	within 1500 bp of TSS
cg23199873	chr7: 93090748	<i>CALCR</i>	-0.045 (0.009)	1.06E-05	0.03	not tested	not tested	Open Sea	within gene body
cg24214000	chr22: 50282386	<i>ZBED4</i>	0.021 (0.004)	1.04E-05	0.03	no	no	South Shelf	3'UTR
cg24954207	chr3: 128217091	NA	-0.039 (0.008)	1.07E-05	0.03	no	no	South Shore	
cg11835347	chr1: 113248232	<i>RHOC</i>	-0.054 (0.011)	1.09E-05	0.04	yes	no	North Shore	5'UTR
cg14457284	chr9: 135852984	<i>GFI1B</i>	-0.04 (0.008)	1.09E-05	0.04	no	no	Open Sea	within 1500 bp of TSS

cg03498271	chr5: 38427885	<i>EGFLAM</i>	-0.055 (0.012)	1.12E-05	0.04	not tested	not tested	Open Sea	within gene body
cg15228983	chr19: 42582914	<i>ZNF574</i>	0.026 (0.005)	1.12E-05	0.04	no	no	North Shore	within gene body
cg07164136	chr10: 108393920	<i>SORCS1</i>	-0.025 (0.005)	1.13E-05	0.04	no	no	Open Sea in CpG Island	within gene body
cg10043090	chr11: 1536810	<i>HCCA2</i>	-0.047 (0.01)	1.14E-05	0.04	no	no	Island	within gene body
cg09554514	chr4: 186693893	<i>SORBS2</i>	-0.036 (0.008)	1.16E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg11482105	chr1: 56241150	NA	-0.033 (0.007)	1.17E-05	0.04	not tested	not tested	Open Sea	
cg13019856	chr2: 70945292	<i>ADD2</i>	-0.042 (0.009)	1.17E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg20907456	chr11: 57405372	NA	-0.029 (0.006)	1.17E-05	0.04	yes	no	Open Sea	
cg13846358	chr9: 135115582	<i>NTNG2</i>	0.032 (0.007)	1.18E-05	0.04	no	no	North Shore	within gene body
cg00216061	chr16: 88547579	<i>ZFPM1</i>	0.025 (0.005)	1.19E-05	0.04	no	no	Open Sea	within gene body
cg14174894	chr19: 42557118	<i>GRIK5</i>	0.023 (0.005)	1.19E-05	0.04	not tested	not tested	Open Sea	within gene body
cg03388769	chr5: 60622671	NA	0.032 (0.007)	1.22E-05	0.04	not tested	not tested	North Shelf	
cg13697368	chr17: 7833663	<i>TRAPPC1</i>	0.02 (0.004)	1.21E-05	0.04	no	no	North Shore	3'UTR
cg26877588	chr18: 61455379	<i>SERPINB7</i>	0.019 (0.004)	1.21E-05	0.04	no	no	Open Sea	within gene body
cg08188318	chr6: 34984953	<i>ANKS1A</i>	-0.093 (0.02)	1.24E-05	0.04	no	no	Open Sea	within gene body
cg12474404	chr14: 102814892	<i>CINP</i>	0.022 (0.005)	1.24E-05	0.04	not tested	not tested	Open Sea	3'UTR
cg12840850	chr20: 62407352	<i>ZBTB46</i>	0.021 (0.005)	1.24E-05	0.04	no	no	South Shore in CpG Island	within gene body
cg27250841	chr18: 47813745	<i>CXXC1</i>	-0.012 (0.003)	1.24E-05	0.04	no	no	Island	within gene body
cg00535807	chr9: 5186210	<i>INSL6</i>	0.015 (0.003)	1.31E-05	0.04	not tested	not tested	South Shore	within 1500 bp of TSS
cg00718684	chr6: 31692026	<i>C6orf25</i>	0.041 (0.009)	1.33E-05	0.04	no	no	South Shore	within gene body
cg01078446	chr12: 115113212	<i>TBX3</i>	-0.05 (0.01)	1.31E-05	0.04	no	no	South Shore	within gene body
cg01327863	chr11: 64878267	<i>TM7SF2</i>	-0.028 (0.006)	1.30E-05	0.04	not tested	not tested	North Shore	within 1500 bp of TSS
cg01461514	chr7: 55177182	<i>EGFR</i>	-0.044 (0.009)	1.26E-05	0.04	no	no	Open Sea	within gene body
cg04009045	chr2: 74804817	<i>M1AP</i>	-0.027 (0.006)	1.27E-05	0.04	not tested	not tested	Open Sea	within gene body
cg04179940	chr20: 33871836	<i>EIF6</i>	-0.032 (0.007)	1.34E-05	0.04	yes	no	North Shore	within gene body
cg06042828	chr16: 68058281	<i>DDX28</i>	-0.022 (0.005)	1.34E-05	0.04	no	no	South Shore	within 1500 bp of TSS

cg07520586	chr17: 2861947	<i>RAP1GAP2</i>	0.022 (0.005)	1.32E-05	0.04	not tested	not tested	Open Sea	within gene body
cg08356805	chr16: 88979098	<i>CBFA2T3</i>	0.023 (0.005)	1.29E-05	0.04	no	no	South Shelf	5'UTR
cg08509749	chr13: 65884209	NA	0.028 (0.006)	1.34E-05	0.04	no	no	Open Sea	
cg09396490	chr9: 126372395	<i>DENND1A</i>	0.02 (0.004)	1.34E-05	0.04	not tested	not tested	Open Sea	within gene body
cg10271993	chr8: 110593242	<i>SYBU</i>	-0.034 (0.007)	1.32E-05	0.04	not tested	not tested	Open Sea	within gene body
cg14561649	chr2: 240044446	<i>HDAC4</i>	0.025 (0.005)	1.31E-05	0.04	not tested	not tested	North Shore	within gene body
cg15547507	chr2: 232557565	NA	0.023 (0.005)	1.28E-05	0.04	not tested	not tested	Open Sea	
cg16049584	chr10: 93735638	<i>BTAF1</i>	0.011 (0.002)	1.31E-05	0.04	not tested	not tested	Open Sea	within gene body
cg18670934	chr8: 128512692	NA	0.013 (0.003)	1.32E-05	0.04	not tested	not tested	Open Sea	
cg19890584	chr13: 100024488	<i>UBAC2</i>	-0.04 (0.008)	1.31E-05	0.04	not tested	not tested	Open Sea	within gene body
cg20538322	chr12: 114851913	NA	0.028 (0.006)	1.29E-05	0.04	no	no	North Shore	
cg06297541	chr16: 22384949	<i>CDR2</i>	-0.053 (0.011)	1.35E-05	0.04	no	no	North Shore	within gene body
cg01593812	chr21: 35312645	<i>LINC00649</i>	-0.033 (0.007)	1.36E-05	0.04	not tested	not tested	Open Sea	within gene body
cg04270823	chr20: 62687554	<i>TCEA2</i>	-0.044 (0.009)	1.36E-05	0.04	not tested	not tested	North Shore	within 1500 bp of TSS
cg10835711	chr8: 77618141	<i>ZFHX4</i>	0.031 (0.007)	1.37E-05	0.04	no	no	Open Sea	within gene body
cg12983664	chr13: 110441015	NA	-0.047 (0.01)	1.38E-05	0.04	not tested	not tested	South Shore	
cg14018648	chr17: 7083015	<i>ASGR1</i>	-0.03 (0.006)	1.40E-05	0.04	no	no	Open Sea	within 200 bp of TSS
cg19933810	chr16: 1386290	<i>BAIAP3</i>	-0.031 (0.007)	1.41E-05	0.04	not tested	not tested	South Shore	5'UTR
cg23383111	chr15: 51742890	<i>DMXL2</i>	0.018 (0.004)	1.41E-05	0.04	not tested	not tested	Open Sea	within gene body
cg24418941	chr19: 2062522	NA	0.028 (0.006)	1.40E-05	0.04	yes	no	South Shore	
cg21019063	chr15: 98065112	<i>LOC101927286</i>	-0.048 (0.01)	1.42E-05	0.04	not tested	not tested	Open Sea	within 200 bp of TSS
cg08548535	chr4: 155661052	NA	0.014 (0.003)	1.43E-05	0.04	no	no	North Shore	
cg08813149	chr1: 192736213	NA	-0.016 (0.004)	1.43E-05	0.04	not tested	not tested	Open Sea	
cg13805711	chr4: 6374101	<i>PPP2R2C</i>	0.024 (0.005)	1.44E-05	0.04	not tested	not tested	Open Sea	within gene body
cg04339947	chr11: 61443052	NA	0.028 (0.006)	1.46E-05	0.04	no	no	Open Sea	
cg06980173	chr1: 154376344	<i>IL6R</i>	-0.047 (0.01)	1.47E-05	0.04	yes	no	North Shore	within 1500 bp of TSS
cg07169009	chr20: 1607919	NA	0.026 (0.006)	1.47E-05	0.04	not tested	not tested	Open Sea	
cg14187236	chr17: 49205442	NA	0.022 (0.005)	1.47E-05	0.04	not tested	not tested	Open Sea	

cg10075503	chr19: 752097	<i>MISP</i>	0.018 (0.004)	1.49E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg10635343	chr5: 39378426	<i>DAB2</i>	0.009 (0.002)	1.49E-05	0.04	not tested	not tested	Open Sea	within gene body
cg12122387	chr8: 17756185	NA	-0.041 (0.008)	1.49E-05	0.04	not tested	not tested	Open Sea	
cg00764771	chr7: 150086034	<i>ZNF775</i>	-0.047 (0.01)	1.55E-05	0.04	not tested	not tested	Open Sea	within gene body
cg03627489	chr16: 51341199	NA	-0.033 (0.007)	1.54E-05	0.04	no	no	Open Sea	
cg04474832	chr3: 52008487	<i>ABHD14B</i>	-0.032 (0.007)	1.51E-05	0.04	no	no	North Shore	within 1st exon
cg04959662	chr2: 109941286	<i>SH3RF3</i>	0.009 (0.002)	1.57E-05	0.04	not tested	not tested	Open Sea	within gene body
cg08879394	chr7: 111162222	<i>IMMP2L</i>	0.013 (0.003)	1.53E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg08971940	chr10: 36214839	NA	0.016 (0.003)	1.54E-05	0.04	no	no	Open Sea	
cg09295164	chr11: 85904644	NA	-0.006 (0.001)	1.58E-05	0.04	not tested	not tested	Open Sea	
cg11474135	chr4: 113933301	<i>ANK2</i>	-0.047 (0.01)	1.51E-05	0.04	no	no	Open Sea	within gene body
cg14155327	chr4: 87235054	<i>MAPK10</i>	-0.04 (0.009)	1.57E-05	0.04	no	no	Open Sea	5'UTR
cg14323608	chr19: 13873961	<i>MRI1</i>	0.028 (0.006)	1.57E-05	0.04	no	no	North Shore	within 1500 bp of TSS
cg17433369	chr9: 129938408	<i>RALGPS1</i>	-0.014 (0.003)	1.57E-05	0.04	not tested	not tested	Open Sea	within gene body
cg21156439	chr9: 94716496	NA	0.051 (0.011)	1.57E-05	0.04	no	no	South Shelf	
cg23222717	chr6: 46462509	NA	0.027 (0.006)	1.52E-05	0.04	no	no	South Shelf	
cg26918607	chr2: 216312473	NA	-0.039 (0.008)	1.56E-05	0.04	not tested	not tested	Open Sea	
cg27260887	chr12: 52435577	<i>NR4A1</i>	-0.029 (0.006)	1.51E-05	0.04	not tested	not tested	South Shelf	within gene body
cg07775790	chr5: 169145735	<i>DOCK2</i>	0.009 (0.002)	1.58E-05	0.04	not tested	not tested	Open Sea	within gene body
cg27418500	chr2: 123758682	NA	0.021 (0.005)	1.59E-05	0.04	no	no	Open Sea	
cg01089519	chr11: 46686440	<i>ATG13</i>	0.02 (0.004)	1.62E-05	0.04	not tested	not tested	Open Sea	within gene body
cg01154210	chr21: 27493310	<i>APP</i>	0.102 (0.022)	1.63E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg02719154	chr4: 111533823	NA	-0.033 (0.007)	1.62E-05	0.04	no	no	South Shore	
cg10504000	chr11: 2402391	<i>CD81</i>	-0.04 (0.009)	1.63E-05	0.04	no	no	South Shelf	within gene body
cg11937241	chr4: 135122152	<i>PABPC4L</i>	0.028 (0.006)	1.63E-05	0.04	no	no	Open Sea	within gene body
cg20500791	chr7: 50420285	<i>IKZF1</i>	-0.042 (0.009)	1.61E-05	0.04	not tested	not tested	Open Sea	within gene body
cg12380764	chr1: 206971195	<i>IL19</i>	-0.039 (0.008)	1.65E-05	0.04	no	no	Open Sea	within 1500 bp of TSS
cg02098967	chr2: 241990667	<i>SNED1</i>	0.023 (0.005)	1.66E-05	0.04	not tested	not tested	North Shore	within gene body
cg04946588	chr7: 86271783	<i>GRM3</i>	-0.052 (0.011)	1.66E-05	0.04	not tested	not tested	Open Sea	within 1500 bp of TSS

cg00082998	chr19: 4008627	<i>PIAS4</i>	-0.027 (0.006)	1.69E-05	0.04	not tested	not tested	South Shore	within gene body
cg01761595	chr8: 9821723	NA	-0.069 (0.015)	1.70E-05	0.04	no	no	Open Sea	
cg02884943	chr10: 72725905	NA	-0.059 (0.013)	1.71E-05	0.04	not tested	not tested	Open Sea	
cg04953061	chr14: 53620393	<i>DDHD1</i>	-0.028 (0.006)	1.73E-05	0.04	no	no	South Shore	within 1500 bp of TSS
cg05703302	chr1: 16279468	<i>ZBTB17</i>	-0.03 (0.006)	1.71E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg09199598	chr17: 3461480	<i>TRPV3</i>	0.022 (0.005)	1.68E-05	0.04	no	no	Open Sea	within 200 bp of TSS
cg11895950	chrX: 44732372	<i>KDM6A</i>	0.002 (0)	1.72E-05	0.04	no	no	Island	within 200 bp of TSS
cg14112754	chr3: 194118613	<i>GP5</i>	-0.039 (0.008)	1.70E-05	0.04	no	no	Island	within gene body
cg16170878	chr13: 49659276	<i>FNDC3A</i>	-0.035 (0.008)	1.70E-05	0.04	not tested	not tested	Open Sea	within gene body
cg18018385	chr10: 101964284	<i>CHUK</i>	0.016 (0.004)	1.72E-05	0.04	not tested	not tested	Open Sea	within gene body
cg26338757	chr10: 88428295	<i>LDB3</i>	-0.037 (0.008)	1.70E-05	0.04	no	no	Open Sea	within 200 bp of TSS
cg26915384	chr16: 27896619	<i>GSG1L</i>	-0.01 (0.002)	1.71E-05	0.04	no	no	Open Sea	within gene body
cg06835772	chr16: 85296220	NA	-0.035 (0.008)	1.76E-05	0.04	yes	no	Open Sea	
cg14827165	chr19: 17221420	<i>MYO9B</i>	-0.025 (0.005)	1.76E-05	0.04	not tested	not tested	Open Sea	within gene body
cg20170309	chr16: 50753273	<i>NOD2</i>	0.021 (0.005)	1.76E-05	0.04	not tested	not tested	Open Sea	within gene body
cg11170796	chr19: 1650224	<i>TCF3</i>	0.024 (0.005)	1.78E-05	0.04	no	no	South Shelf	within gene body
cg02202721	chr1: 156865043	<i>PEAR1</i>	-0.033 (0.007)	1.79E-05	0.04	not tested	not tested	South Shore	5'UTR
cg14425843	chr7: 92729833	<i>SAMD9</i>	0.012 (0.003)	1.79E-05	0.04	no	no	Open Sea	3'UTR
cg08319238	chr19: 45312525	<i>BCAM</i>	-0.025 (0.005)	1.82E-05	0.04	no	no	South Shore	within gene body
cg11673291	chr1: 36787145	NA	-0.035 (0.008)	1.81E-05	0.04	no	no	Island	
cg22665096	chr12: 42102842	NA	-0.02 (0.004)	1.82E-05	0.04	no	no	Open Sea	
cg24437293	chr19: 2065374	NA	0.027 (0.006)	1.83E-05	0.04	no	no	South Shore	
cg22191973	chr18: 55292558	NA	0.021 (0.005)	1.84E-05	0.04	no	no	South Shelf	
cg17885233	chr3: 132450221	<i>NPHP3-AS1</i>	-0.051 (0.011)	1.84E-05	0.04	not tested	not tested	Open Sea	within gene body
cg14396995	chr7: 42278089	<i>GLI3</i>	0.06 (0.013)	1.86E-05	0.04	no	no	South Shore	within 1500 bp of TSS
cg04157263	chr17: 37752991	NA	-0.027 (0.006)	1.87E-05	0.04	no	no	Island	
cg07131742	chr11: 66112880	<i>B3GNT1</i>	-0.041 (0.009)	1.89E-05	0.04	no	no	North Shore	3'UTR
cg12423902	chr6: 30159309	<i>TRIM26</i>	0.013 (0.003)	1.89E-05	0.04	no	no	Open Sea	within gene body

cg13962771	chr5: 140048068	<i>WDR55</i>	0.019 (0.004)	1.90E-05	0.04	not tested	not tested	South Shelf	within gene body
cg03917515	chr16: 53465339	NA	0.017 (0.004)	1.91E-05	0.04	no	no	North Shelf	
cg04552136	chr22: 50656153	<i>TUBGCP6</i>	0.02 (0.004)	1.91E-05	0.04	no	no	North Shore	3'UTR
cg05454781	chr1: 10651344	<i>PEX14</i>	-0.034 (0.007)	1.91E-05	0.04	not tested	not tested	Open Sea	within gene body
cg10142738	chr11: 19757625	<i>NAV2</i>	-0.035 (0.008)	1.93E-05	0.04	not tested	not tested	Open Sea	within gene body
cg15472784	chr1: 3663531	<i>KIAA0495</i>	-0.003 (0.001)	1.93E-05	0.04	no	no	in CpG Island	within 1st exon
cg21801962	chr1: 57602295	<i>DAB1</i>	0.02 (0.004)	1.94E-05	0.04	not tested	not tested	Open Sea	ExonBnd
cg01530448	chr21: 36319162	<i>RUNX1</i>	0.011 (0.003)	1.94E-05	0.04	not tested	not tested	Open Sea	within gene body
cg06596521	chr3: 126263868	<i>C3orf22</i>	-0.042 (0.009)	1.95E-05	0.04	not tested	not tested	South Shelf	within gene body
cg12836643	chr22: 39129370	<i>GTPBP1</i>	-0.03 (0.007)	1.95E-05	0.04	yes	yes	Open Sea	3'UTR
cg18073938	chr4: 100789493	<i>DAPP1</i>	-0.032 (0.007)	1.97E-05	0.04	not tested	not tested	Open Sea	3'UTR
cg21034201	chr18: 33160855	NA	-0.021 (0.005)	1.96E-05	0.04	not tested	not tested	North Shore	
cg21844291	chr2: 11097873	NA	-0.029 (0.006)	1.98E-05	0.04	no	no	North Shelf	
cg10058373	chr10: 120766572	NA	-0.032 (0.007)	2.00E-05	0.04	not tested	not tested	Open Sea	
cg27056175	chr8: 141556352	<i>EIF2C2</i>	0.006 (0.001)	2.01E-05	0.04	no	no	North Shelf	within gene body
cg00102795	chr10: 3151915	<i>PFKP</i>	0.017 (0.004)	2.05E-05	0.04	not tested	not tested	South Shelf	within gene body
cg15909006	chr16: 2086421	<i>SLC9A3R2</i>	0.026 (0.006)	2.06E-05	0.04	no	no	in CpG Island	within gene body
cg21886561	chr12: 53730326	<i>SP7</i>	-0.024 (0.005)	2.07E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg15187175	chr13: 94176949	<i>GPC6</i>	0.021 (0.005)	2.08E-05	0.04	no	no	Open Sea	within gene body
cg00441550	chr20: 29955998	<i>DEFB118</i>	-0.06 (0.013)	2.21E-05	0.04	not tested	not tested	Open Sea	within 1500 bp of TSS
cg01052743	chr8: 128747083	<i>MYC</i>	0.006 (0.001)	2.47E-05	0.04	no	no	North Shore	within 1500 bp of TSS
cg01260075	chr17: 28620354	<i>BLMH</i>	0.015 (0.003)	2.31E-05	0.04	not tested	not tested	South Shore	within 1500 bp of TSS
cg02147126	chr19: 827715	<i>AZU1</i>	-0.031 (0.007)	2.35E-05	0.04	no	no	Open Sea	within 200 bp of TSS
cg02956226	chr17: 4917032	<i>KIF1C</i>	0.016 (0.004)	2.19E-05	0.04	not tested	not tested	Open Sea	ExonBnd
cg03435866	chr2: 30452607	NA	0.009 (0.002)	2.28E-05	0.04	no	no	North Shore	
cg03520471	chr3: 97753623	<i>GABRR3</i>	-0.054 (0.012)	2.30E-05	0.04	no	no	Open Sea	within gene body
cg03678999	chr1: 1912135	<i>CFAP74</i>	0.023 (0.005)	2.47E-05	0.04	not tested	not tested	in CpG Island	within gene body

cg04708601	chr6: 101880078	<i>GRIK2</i>	-0.051 (0.011)	2.19E-05	0.04	no	no	Open Sea	within gene body
cg05002615	chr7: 68326108	NA	0.005 (0.001)	2.22E-05	0.04	no	no	Open Sea	
cg05233535	chr12: 6497969	<i>LTBR</i>	0.015 (0.003)	2.42E-05	0.04	not tested	not tested	Open Sea	within gene body
cg05293706	chr2: 219194675	<i>PNKD</i>	-0.036 (0.008)	2.24E-05	0.04	not tested	not tested	Open Sea	within gene body
cg05370277	chr4: 10006097	<i>SLC2A9</i>	0.019 (0.004)	2.12E-05	0.04	not tested	not tested	Open Sea	within gene body
cg05516255	chr15: 75652110	<i>MAN2C1</i>	0.023 (0.005)	2.38E-05	0.04	not tested	not tested	South Shelf	within gene body
cg05712904	chr19: 2692137	<i>GNG7</i>	0.023 (0.005)	2.46E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg05731156	chr16: 30418364	<i>ZNF771</i>	-0.01 (0.002)	2.28E-05	0.04	no	no	North Shore	within 1500 bp of TSS
cg05797982	chr5: 71764958	<i>ZNF366</i>	-0.041 (0.009)	2.19E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg05990312	chr17: 19628421	NA	-0.036 (0.008)	2.37E-05	0.04	no	no	South Shore	
cg07064050	chr19: 19165011	<i>ARMC6</i>	0.025 (0.006)	2.18E-05	0.04	no	no	Open Sea	within gene body
cg07126444	chr14: 75608010	<i>TMED10</i>	-0.047 (0.01)	2.34E-05	0.04	not tested	not tested	Open Sea	within gene body
cg07511317	chr14: 104159997	<i>KLC1</i>	0.014 (0.003)	2.47E-05	0.04	no	no	Open Sea	within gene body
cg08257567	chr3: 46009762	<i>FYCO1</i>	0.019 (0.004)	2.41E-05	0.04	not tested	not tested	Open Sea	within gene body
cg08343999	chr21: 43635188	<i>ABCG1</i>	0.019 (0.004)	2.26E-05	0.04	not tested	not tested	North Shelf	within 1500 bp of TSS
cg08743392	chr20: 33543028	<i>GSS</i>	-0.027 (0.006)	2.41E-05	0.04	no	no	North Shore	5'UTR
cg08811516	chr13: 35043968	<i>LINC00457</i>	-0.04 (0.009)	2.40E-05	0.04	not tested	not tested	Open Sea	within gene body
cg09023892	chr22: 38072101	<i>LGALS1</i>	-0.033 (0.007)	2.47E-05	0.04	not tested	not tested	North Shore	within gene body
cg09060489	chr1: 27874526	<i>AHDC1</i>	0.025 (0.006)	2.46E-05	0.04	no	no	in CpG Island	within gene body
cg09953898	chr2: 8935087	<i>KIDINS220</i>	-0.044 (0.01)	2.28E-05	0.04	not tested	not tested	Open Sea	within gene body
cg10370599	chr16: 22825158	<i>HS3ST2</i>	-0.004 (0.001)	2.40E-05	0.04	no	no	in CpG Island	within 1500 bp of TSS
cg11599849	chr1: 48809125	<i>SPATA6</i>	0.016 (0.003)	2.28E-05	0.04	not tested	not tested	Open Sea	within gene body
cg11980819	chr19: 4302579	<i>TMIGD2</i>	-0.026 (0.006)	2.22E-05	0.04	yes	no	North Shore	within 200 bp of TSS
cg12063619	chr13: 92868702	<i>GPC5</i>	-0.046 (0.01)	2.45E-05	0.04	not tested	not tested	Open Sea	within gene body
cg12249789	chr21: 45203404	NA	0.036 (0.008)	2.42E-05	0.04	yes	no	North Shelf	
cg12568707	chr19: 19042904	<i>HOMER3</i>	0.021 (0.005)	2.31E-05	0.04	no	no	in CpG Island	within gene body



cg12973855	chr15: 59816483	NA	-0.038 (0.008)	2.13E-05	0.04	not tested	not tested	Open Sea	
cg13657983	chr5: 73405407	NA	0.021 (0.005)	2.39E-05	0.04	not tested	not tested	Open Sea	
cg14153927	chr19: 46846465	<i>HIF3A</i>	-0.032 (0.007)	2.29E-05	0.04	no	no	North Shelf	3'UTR within 1500 bp of TSS
cg14374920	chr11: 57996779	<i>OR10Q1</i>	0.011 (0.003)	2.46E-05	0.04	not tested	not tested	Open Sea	
cg15059075	chr19: 30264378	NA	0.023 (0.005)	2.33E-05	0.04	not tested	not tested	Open Sea	
cg15235434	chr1: 171197048	NA	0.015 (0.003)	2.42E-05	0.04	not tested	not tested	Open Sea	
cg15701979	chr4: 20554680	<i>SLIT2</i>	0.024 (0.005)	2.46E-05	0.04	not tested	not tested	Open Sea	within gene body
cg16145176	chr21: 25596030	NA	-0.06 (0.013)	2.32E-05	0.04	not tested	not tested	Open Sea	
cg16350196	chr4: 137426420	NA	-0.052 (0.011)	2.36E-05	0.04	not tested	not tested	Open Sea	
cg16524284	chr19: 33353338	<i>SLC7A9</i>	0.027 (0.006)	2.15E-05	0.04	no	no	South Shelf	within gene body
cg16713094	chr9: 99450648	NA	0.021 (0.005)	2.14E-05	0.04	not tested	not tested	South Shore	
cg18713358	chr11: 67038249	<i>ADRBK1</i>	-0.028 (0.006)	2.26E-05	0.04	not tested	not tested	South Shelf	within gene body
cg19190900	chr2: 37553621	NA	0.053 (0.012)	2.23E-05	0.04	no	no	South Shore	
cg19194448	chr2: 178976361	<i>RBM45</i>	0.012 (0.003)	2.09E-05	0.04	no	no	North Shore	within 1500 bp of TSS
cg20142271	chr4: 81106287	<i>PRDM8</i>	-0.005 (0.001)	2.30E-05	0.04	no	no	South Shore	within 200 bp of TSS within gene body
cg20637770	chr1: 212872225	<i>BATF3</i>	-0.027 (0.006)	2.36E-05	0.04	not tested	not tested	North Shore	
cg20736045	chr8: 146270290	NA	-0.039 (0.009)	2.44E-05	0.04	not tested	not tested	Open Sea	
cg21016438	chr1: 109843435	<i>MYBPHL</i>	-0.031 (0.007)	2.44E-05	0.04	not tested	not tested	Open Sea	within gene body
cg21165486	chr1: 165606857	<i>MGST3</i>	-0.034 (0.008)	2.10E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg21386863	chr2: 150977022	NA	-0.04 (0.009)	2.23E-05	0.04	no	no	Open Sea	
cg21637741	chr8: 69834365	<i>LINC01592</i>	-0.052 (0.011)	2.40E-05	0.04	not tested	not tested	Open Sea	within gene body
cg21721331	chr1: 157670877	<i>FCRL3</i>	-0.061 (0.013)	2.13E-05	0.04	not tested	not tested	Open Sea	within 1500 bp of TSS
cg21806273	chr1: 247578953	<i>NLRP3</i>	-0.042 (0.009)	2.26E-05	0.04	no	no	Open Sea	within 1500 bp of TSS
cg22059430	chr7: 128346474	NA	0.014 (0.003)	2.14E-05	0.04	not tested	not tested	Open Sea	
cg22549504	chr19: 17448937	<i>GTPBP3</i>	0.001 (0)	2.29E-05	0.04	no	no	in CpG Island	within gene body within 200 bp of TSS
cg22574288	chr9: 22646113	<i>LINC01239</i>	-0.049 (0.011)	2.34E-05	0.04	not tested	not tested	Open Sea	
cg22589055	chr8: 86973512	NA	-0.037 (0.008)	2.27E-05	0.04	not tested	not tested	Open Sea	
cg22686259	chr16: 57984539	<i>CNGB1</i>	-0.034 (0.008)	2.43E-05	0.04	not tested	not tested	Open Sea	within gene body
cg23024158	chr10: 78011952	<i>C10orf11</i>	-0.051 (0.011)	2.36E-05	0.04	yes	no	Open Sea	within gene body

cg25038337	chr8: 141551653	<i>AGO2</i>	-0.017 (0.004)	2.42E-05	0.04	not tested	not tested	Open Sea	within gene body
cg25133376	chr7: 73392981	NA	-0.026 (0.006)	2.25E-05	0.04	no	no	Open Sea	
cg25467652	chr1: 11795976	<i>AGTRAP</i>	-0.034 (0.007)	2.29E-05	0.04	no	no	Open Sea in CpG Island	within 200 bp of TSS within gene body
cg26617588	chr10: 73398446	<i>CDH23</i>	-0.027 (0.006)	2.18E-05	0.04	not tested	not tested	Open Sea in CpG Island	within gene body
cg27496793	chr2: 46926433	<i>SOCS5</i>	0.029 (0.006)	2.21E-05	0.04	no	no	Open Sea in CpG Island	5'UTR within 1st exon
cg14483291	chr11: 17569007	<i>OTOG</i>	-0.042 (0.009)	2.49E-05	0.04	not tested	not tested	South Shelf in CpG Island	within gene body
cg16661234	chr17: 10541620	<i>MYH3</i>	-0.003 (0.001)	2.49E-05	0.04	no	no	Open Sea	within gene body
cg00596184	chr16: 69350052	<i>VPS4A</i>	0.029 (0.006)	2.59E-05	0.04	no	no	Open Sea	within gene body
cg01002322	chr2: 6872536	<i>LINC00487</i>	-0.045 (0.01)	2.56E-05	0.04	not tested	not tested	Open Sea	within gene body
cg01004862	chr16: 67249478	<i>LRRC29</i>	0.021 (0.005)	2.58E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg02395812	chr14: 105955879	<i>C14orf80</i>	-0.036 (0.008)	2.59E-05	0.04	no	no	North Shore	within 1500 bp of TSS within gene body
cg03333101	chr19: 12954349	<i>MAST1</i>	0.023 (0.005)	2.60E-05	0.04	yes	no	North Shelf	
cg03665051	chr22: 37569910	NA	-0.032 (0.007)	2.55E-05	0.04	not tested	not tested	Open Sea	
cg03882382	chr19: 4540065	<i>LRG1</i>	-0.036 (0.008)	2.57E-05	0.04	no	no	North Shelf	within 200 bp of TSS within gene body
cg06390790	chr17: 3654836	<i>ITGAE</i>	0.025 (0.006)	2.58E-05	0.04	yes	no	North Shelf	within gene body
cg07460883	chr11: 65378788	<i>MAP3K11</i>	-0.025 (0.006)	2.54E-05	0.04	not tested	not tested	South Shelf in CpG Island	within gene body
cg08839210	chr17: 27045048	<i>RAB34</i>	-0.027 (0.006)	2.51E-05	0.04	yes	no	Open Sea	within 200 bp of TSS within gene body
cg10126398	chr1: 162825937	<i>C1orf110</i>	0.022 (0.005)	2.51E-05	0.04	no	no	Open Sea	
cg11933019	chr11: 99291687	<i>CNTN5</i>	-0.04 (0.009)	2.57E-05	0.04	no	no	Open Sea	5'UTR
cg15992232	chr20: 59524596	NA	0.021 (0.005)	2.60E-05	0.04	not tested	not tested	Open Sea	
cg16103159	chr22: 26561575	NA	-0.049 (0.011)	2.56E-05	0.04	no	no	North Shelf	
cg16344173	chr7: 2158623	<i>MAD1L1</i>	0.028 (0.006)	2.53E-05	0.04	no	no	South Shelf	within gene body
cg18359017	chr11: 5538958	<i>UBQLNL</i>	-0.039 (0.009)	2.56E-05	0.04	not tested	not tested	Open Sea	within 1500 bp of TSS
cg20141502	chr16: 28922391	<i>RABEP2</i>	0.018 (0.004)	2.52E-05	0.04	not tested	not tested	Open Sea	ExonBnd
cg26387796	chr7: 150147927	<i>GIMAP8</i>	-0.011 (0.002)	2.60E-05	0.04	no	no	Open Sea in CpG Island	within 200 bp of TSS within gene body
cg01940336	chr19: 47935484	<i>SLC8A2</i>	0.022 (0.005)	2.62E-05	0.04	no	no	Open Sea in CpG Island	within gene body

cg26610808	chr10: 102046685	<i>BLOC1S2</i>	-0.039 (0.009)	2.62E-05	0.04	yes	no	South Shore	within 1500 bp of TSS
cg20788793	chr20: 3773402	NA	0.008 (0.002)	2.63E-05	0.04	no	no	North Shelf in CpG Island	
cg03839949	chr3: 128210541	<i>GATA2</i>	-0.023 (0.005)	2.66E-05	0.04	no	no	Open Sea	5'UTR within 1st exon
cg23241914	chr1: 161193393	<i>APOA2</i>	0.019 (0.004)	2.66E-05	0.04	no	no	Open Sea	within 1st exon
cg25944620	chr10: 75401315	<i>MYOZ1</i>	0.019 (0.004)	2.66E-05	0.04	no	no	Open Sea	within 1500 bp of TSS
cg08473663	chr17: 26695438	<i>SEBOX</i>	0.016 (0.004)	2.67E-05	0.04	no	no	North Shelf	within gene body
cg15591386	chr1: 76265299	<i>MSH4</i>	-0.054 (0.012)	2.67E-05	0.04	no	no	South Shelf	
cg10387848	chr18: 29757472	NA	-0.036 (0.008)	2.69E-05	0.04	not tested	not tested	Open Sea	
cg14426913	chr6: 6956252	NA	0.026 (0.006)	2.69E-05	0.04	no	no	Open Sea	
cg02938807	chr14: 63785523	<i>GPHB5</i>	-0.069 (0.015)	2.72E-05	0.04	no	no	Open Sea	within 1500 bp of TSS
cg04572631	chr3: 158565194	NA	-0.028 (0.006)	2.72E-05	0.04	not tested	not tested	Open Sea	
cg08491668	chr6: 32935236	<i>BRD2</i>	-0.03 (0.007)	2.72E-05	0.04	no	no	North Shore	within 1500 bp of TSS
cg09917488	chr19: 39635460	<i>PAK4</i>	-0.027 (0.006)	2.72E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg10420626	chr6: 43741154	<i>VEGFA</i>	-0.057 (0.013)	2.72E-05	0.04	not tested	not tested	South Shore	5'UTR within gene body
cg15850010	chr1: 170690670	<i>PRRX1</i>	-0.03 (0.007)	2.73E-05	0.04	not tested	not tested	Open Sea	within 200 bp of TSS
cg12463158	chr7: 150902745	<i>IQCA1L</i>	0.014 (0.003)	2.75E-05	0.04	not tested	not tested	South Shore	within gene body
cg00612202	chr7: 926974	<i>C7orf20</i>	0.024 (0.005)	2.79E-05	0.04	no	no	North Shelf	within gene body
cg00666124	chr2: 54756403	<i>RPL23AP32</i>	0.011 (0.002)	2.86E-05	0.04	no	no	Open Sea	within gene body
cg00770158	chr3: 57134628	<i>IL17RD</i>	-0.027 (0.006)	2.98E-05	0.04	no	no	South Shelf	within gene body
cg01035334	chr11: 117883077	NA	-0.033 (0.008)	3.15E-05	0.04	not tested	not tested	Open Sea	
cg01598569	chr11: 130500748	NA	-0.026 (0.006)	3.05E-05	0.04	not tested	not tested	Open Sea	
cg01619618	chr1: 23610607	<i>LINC01355</i>	-0.024 (0.005)	3.13E-05	0.04	not tested	not tested	Open Sea	within gene body
cg01658960	chr12: 132690570	<i>GALNT9</i>	-0.04 (0.009)	2.80E-05	0.04	no	no	in CpG Island	within gene body
cg02053339	chr22: 43088726	<i>A4GALT</i>	0.028 (0.006)	2.86E-05	0.04	no	no	North Shore	3'UTR
cg02078604	chr1: 8797440	<i>RERE</i>	-0.042 (0.009)	3.01E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg02081718	chr6: 88300968	<i>RARS2</i>	0.014 (0.003)	3.14E-05	0.04	not tested	not tested	South Shore	within 1500 bp of TSS

cg03140624	chr1: 235931377	<i>LYST</i>	-0.049 (0.011)	3.09E-05	0.04	no	no	Open Sea	within gene body
cg03529447	chr9: 133274183	<i>HMCN2</i>	0.019 (0.004)	3.13E-05	0.04	not tested	not tested	Open Sea	within gene body
cg03638795	chr11: 416499	<i>SIGIRR</i>	-0.04 (0.009)	3.06E-05	0.04	yes	yes	Open Sea in CpG Island	5'UTR
cg03665908	chr19: 17631991	<i>PGLS</i>	0.03 (0.007)	3.07E-05	0.04	no	no	Open Sea in CpG Island	3'UTR
cg04262465	chr14: 101405693	<i>SNORD113-6</i>	-0.039 (0.009)	2.91E-05	0.04	no	no	Open Sea	within 200 bp of TSS
cg04528240	chr4: 56504657	NA	-0.017 (0.004)	3.15E-05	0.04	no	no	South Shelf	
cg04609640	chr1: 45254092	<i>BEST4</i>	-0.035 (0.008)	3.15E-05	0.04	no	no	South Shore	within 1500 bp of TSS
cg04728045	chr11: 111298336	NA	-0.048 (0.011)	2.90E-05	0.04	not tested	not tested	Open Sea	
cg04742397	chr14: 95986554	NA	-0.034 (0.008)	2.82E-05	0.04	yes	no	South Shelf	
cg05094137	chr16: 53125208	<i>CHD9</i>	-0.028 (0.006)	3.14E-05	0.04	no	no	Open Sea	5'UTR
cg05256584	chr2: 40452795	<i>SLC8A1</i>	0.021 (0.005)	3.03E-05	0.04	no	no	Open Sea	within gene body
cg06525670	chr13: 30528708	NA	-0.041 (0.009)	2.93E-05	0.04	no	no	Open Sea	
cg06823863	chr16: 19296692	<i>LOC728276</i>	0.013 (0.003)	2.88E-05	0.04	no	no	Open Sea	within 1500 bp of TSS
cg06887251	chr5: 67576008	<i>PIK3R1</i>	-0.054 (0.012)	2.83E-05	0.04	not tested	not tested	Open Sea	within gene body
cg06923291	chr12: 90456743	NA	-0.038 (0.008)	2.97E-05	0.04	not tested	not tested	Open Sea	
cg07666998	chr4: 8254585	NA	-0.04 (0.009)	3.07E-05	0.04	not tested	not tested	Open Sea	
cg08202553	chr19: 36156064	<i>UPK1A</i>	0.013 (0.003)	3.13E-05	0.04	not tested	not tested	Open Sea	within 1500 bp of TSS
cg08301307	chr14: 103599204	<i>TNFAIP2</i>	0.019 (0.004)	2.90E-05	0.04	no	no	Open Sea	within gene body
cg08450168	chr1: 28918231	<i>RAB42</i>	0.02 (0.005)	2.84E-05	0.04	no	no	North Shore	within 1500 bp of TSS
cg09427273	chr10: 11077625	<i>CUGBP2</i>	-0.028 (0.006)	3.16E-05	0.04	no	no	Open Sea	within gene body
cg09780594	chr9: 96576175	NA	-0.032 (0.007)	3.08E-05	0.04	not tested	not tested	Open Sea	
cg10153638	chr3: 156835317	<i>LINC00880</i>	-0.044 (0.01)	3.15E-05	0.04	not tested	not tested	North Shelf	within gene body
cg10232265	chr10: 126782326	<i>CTBP2</i>	0.026 (0.006)	2.83E-05	0.04	no	no	Open Sea	5'UTR
cg10428881	chr14: 81770194	<i>STON2</i>	-0.036 (0.008)	3.11E-05	0.04	not tested	not tested	Open Sea	within gene body
cg10698419	chr4: 72897317	<i>NPFFR2</i>	0.021 (0.005)	3.11E-05	0.04	no	no	North Shore	within 1500 bp of TSS
cg11579421	chr10: 134211857	<i>PWWP2B</i>	-0.041 (0.009)	3.02E-05	0.04	no	no	South Shore	within gene body

cg11902424	chr5: 2252995	NA	0.043 (0.01)	3.11E-05	0.04	no	no	Open Sea	
cg12157761	chr15: 71005778	<i>UACA</i>	-0.039 (0.009)	2.99E-05	0.04	no	no	Open Sea	within gene body
cg12234652	chr19: 35811489	NA	-0.026 (0.006)	3.14E-05	0.04	not tested	not tested	Open Sea	
cg12891543	chr16: 53958626	<i>FTO</i>	-0.052 (0.012)	3.09E-05	0.04	not tested	not tested	Open Sea	within gene body
cg13092082	chr1: 192602520	NA	-0.025 (0.006)	3.02E-05	0.04	no	no	Open Sea	
cg13131168	chr8: 145542119	<i>DGAT1</i>	0.024 (0.005)	3.16E-05	0.04	not tested	not tested	Open Sea	within gene body
cg13537774	chr9: 84088338	NA	0.016 (0.004)	2.91E-05	0.04	no	no	Open Sea	
cg13645530	chr12: 116756948	NA	-0.045 (0.01)	3.14E-05	0.04	yes	yes	Open Sea	
cg15047616	chr22: 27015719	NA	-0.031 (0.007)	2.86E-05	0.04	not tested	not tested	Open Sea	
cg15156528	chr12: 49583981	<i>TUBA1A</i>	-0.037 (0.008)	3.12E-05	0.04	not tested	not tested	South Shore	within 1500 bp of TSS
cg15221794	chr13: 29943389	<i>MTUS2</i>	-0.005 (0.001)	3.10E-05	0.04	not tested	not tested	Open Sea	within gene body
cg15616051	chr3: 122770795	NA	-0.026 (0.006)	2.81E-05	0.04	not tested	not tested	Open Sea	
cg17594681	chr19: 45991739	<i>RTN2</i>	0.024 (0.005)	3.09E-05	0.04	not tested	not tested	Open Sea	within gene body
cg17704620	chr14: 77763369	<i>POMT2</i>	0.014 (0.003)	3.01E-05	0.04	not tested	not tested	Open Sea	within gene body
cg17712081	chr12: 57662315	<i>R3HDM2</i>	-0.024 (0.005)	3.13E-05	0.04	not tested	not tested	Open Sea	within gene body
cg17844178	chr16: 12562911	<i>SNX29</i>	0.009 (0.002)	2.87E-05	0.04	not tested	not tested	Open Sea	within gene body
cg18064897	chrX: 10085184	<i>WWC3</i>	0.028 (0.006)	3.09E-05	0.04	no	no	in CpG Island	within gene body
cg18215449	chr12: 66089473	NA	-0.045 (0.01)	2.90E-05	0.04	no	no	Open Sea	
cg18308901	chr9: 140376822	<i>PNPLA7</i>	-0.028 (0.006)	2.82E-05	0.04	not tested	not tested	South Shore	within gene body
cg18681014	chr14: 105660876	NA	-0.04 (0.009)	3.07E-05	0.04	no	no	North Shore	
cg20300412	chr4: 65749341	NA	-0.064 (0.014)	3.07E-05	0.04	not tested	not tested	Open Sea	
cg20302236	chr8: 28637293	<i>INTS9</i>	-0.028 (0.006)	3.07E-05	0.04	not tested	not tested	Open Sea	within gene body
cg20653075	chr8: 65291682	<i>MIR124-2</i>	-0.024 (0.005)	2.97E-05	0.04	no	no	South Shore	within 200 bp of TSS
cg21359538	chr4: 76440740	<i>RCHY1</i>	-0.062 (0.014)	3.05E-05	0.04	not tested	not tested	South Shore	within 1500 bp of TSS
cg21452013	chr3: 31269300	NA	0.009 (0.002)	2.82E-05	0.04	not tested	not tested	Open Sea	
cg21784411	chr1: 3251502	<i>PRDM16</i>	0.025 (0.006)	2.88E-05	0.04	yes	no	Open Sea	within gene body
cg22239593	chr10: 103540102	<i>FGF8</i>	-0.028 (0.006)	3.06E-05	0.04	not tested	not tested	South Shore	5'UTR
cg22265441	chr15: 58011290	NA	0.013 (0.003)	2.79E-05	0.04	not tested	not tested	Open Sea	

cg22848722	chr10: 80917822	<i>ZMIZ1</i>	-0.037 (0.008)	2.88E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg25921418	chr6: 31621008	<i>BAT3</i>	-0.009 (0.002)	2.99E-05	0.04	no	no	in CpG Island	within 1500 bp of TSS
cg26431261	chr8: 74418384	<i>STAU2</i>	0.017 (0.004)	3.12E-05	0.04	not tested	not tested	Open Sea	within gene body
cg24907814	chr5: 2758088	NA	-0.028 (0.006)	3.17E-05	0.04	no	no	South Shore	
cg06794088	chr19: 19426589	<i>SUGP1</i>	0.026 (0.006)	3.17E-05	0.04	not tested	not tested	Open Sea	within gene body
cg09732711	chr10: 130696072	NA	-0.03 (0.007)	3.18E-05	0.04	no	no	Open Sea	
cg20493821	chr15: 89341999	NA	-0.024 (0.005)	3.21E-05	0.04	not tested	not tested	Open Sea	
cg21688288	chr21: 44181258	<i>PDE9A</i>	0.022 (0.005)	3.22E-05	0.04	no	no	Open Sea in CpG Island	within gene body
cg06168449	chr19: 38714549	<i>DPF1</i>	0.018 (0.004)	3.26E-05	0.05	no	no	Open Sea	within gene body
cg11764535	chr6: 46380623	<i>RCAN2</i>	-0.04 (0.009)	3.25E-05	0.05	not tested	not tested	Open Sea	within gene body
cg01772854	chr5: 1176225	NA	0.031 (0.007)	3.28E-05	0.05	no	no	Open Sea	
cg02329351	chr13: 44977492	<i>TUSC8</i>	-0.019 (0.004)	3.37E-05	0.05	not tested	not tested	Open Sea	within gene body
cg02966624	chr1: 150668227	<i>GOLPH3L</i>	-0.037 (0.008)	3.33E-05	0.05	not tested	not tested	Open Sea	5'UTR
cg03457781	chr3: 20418856	NA	-0.021 (0.005)	3.31E-05	0.05	no	no	Open Sea	
cg04823228	chr5: 176258443	<i>UNC5A</i>	0.024 (0.005)	3.40E-05	0.05	not tested	not tested	Open Sea	within gene body
cg06549111	chr12: 58287804	NA	-0.025 (0.006)	3.39E-05	0.05	not tested	not tested	North Shelf	
cg06679537	chr9: 112210147	<i>PTPN3</i>	-0.027 (0.006)	3.29E-05	0.05	not tested	not tested	Open Sea	within gene body
cg08410015	chr10: 119862094	<i>CASC2</i>	-0.035 (0.008)	3.33E-05	0.05	not tested	not tested	Open Sea in CpG Island	within gene body
cg12817436	chr19: 1068561	<i>HMHA1</i>	-0.023 (0.005)	3.36E-05	0.05	no	no	Open Sea	within 1500 bp of TSS
cg13590419	chr20: 43209782	<i>PKIG</i>	-0.035 (0.008)	3.39E-05	0.05	not tested	not tested	Open Sea	
cg14080033	chr7: 2663085	NA	-0.029 (0.007)	3.40E-05	0.05	not tested	not tested	Open Sea	
cg16994421	chr17: 33569462	<i>SLFN5</i>	-0.005 (0.001)	3.40E-05	0.05	not tested	not tested	in CpG Island	within 1500 bp of TSS
cg18388619	chr17: 1792197	<i>RPA1</i>	0.021 (0.005)	3.36E-05	0.05	no	no	Open Sea	within gene body
cg18841746	chr4: 114681688	<i>CAMK2D</i>	0.005 (0.001)	3.38E-05	0.05	no	no	North Shore	within gene body
cg18964464	chr12: 93741046	<i>LOC643339</i>	-0.031 (0.007)	3.37E-05	0.05	not tested	not tested	Open Sea	within gene body
cg19008646	chr3: 31145476	NA	-0.019 (0.004)	3.33E-05	0.05	no	no	Open Sea	
cg20781421	chr11: 11866554	<i>USP47</i>	-0.033 (0.007)	3.37E-05	0.05	no	no	South Shelf	within gene body

cg23502495	chr16: 3175677	<i>ZNF213-AS1</i>	0.012 (0.003)	3.31E-05	0.05	not tested	not tested	South Shore	within gene body
cg24743838	chr8: 143696464	<i>ARC</i>	-0.029 (0.007)	3.30E-05	0.05	not tested	not tested	South Shore	within 1500 bp of TSS
cg25139718	chr1: 2027575	<i>PRKCZ</i>	0.021 (0.005)	3.37E-05	0.05	no	no	South Shore	within gene body
cg27160460	chr11: 66617512	<i>PC</i>	0.024 (0.005)	3.36E-05	0.05	not tested	not tested	Open Sea	within gene body
cg27509293	chr6: 14919597	NA	-0.057 (0.013)	3.36E-05	0.05	not tested	not tested	Open Sea	
cg00325007	chr9: 5774228	<i>RIC1</i>	0.013 (0.003)	3.41E-05	0.05	not tested	not tested	Open Sea	within gene body
cg07887517	chr17: 79005277	<i>BAIAP2-AS1</i>	-0.034 (0.008)	3.45E-05	0.05	not tested	not tested	North Shore	within gene body
cg11531968	chr4: 73969865	<i>ANKRD17</i>	0.016 (0.004)	3.44E-05	0.05	not tested	not tested	Open Sea	within gene body
cg12342178	chr1: 238282400	NA	-0.022 (0.005)	3.44E-05	0.05	not tested	not tested	Open Sea	
cg11845488	chr14: 70189638	NA	0.011 (0.002)	3.46E-05	0.05	no	no	North Shelf	
cg14293102	chr19: 2232170	<i>DOT1L</i>	0.011 (0.003)	3.47E-05	0.05	no	no	South Shore	3'UTR
cg01370074	chr3: 170902250	<i>TNIK</i>	-0.04 (0.009)	3.53E-05	0.05	not tested	not tested	Open Sea	within gene body
cg10684056	chr8: 128494566	<i>CASC8</i>	-0.022 (0.005)	3.53E-05	0.05	not tested	not tested	Open Sea	within 200 bp of TSS
cg19995259	chr19: 53795827	<i>BIRC8</i>	-0.056 (0.013)	3.53E-05	0.05	not tested	not tested	South Shore	within 1500 bp of TSS
cg23178580	chr11: 6806121	<i>OR2AG1</i>	-0.022 (0.005)	3.53E-05	0.05	not tested	not tested	Open Sea	within 200 bp of TSS
cg26723045	chr11: 9042581	<i>SCUBE2</i>	-0.027 (0.006)	3.52E-05	0.05	no	no	Open Sea	3'UTR
cg10007431	chr14: 89866249	<i>FOXN3</i>	-0.044 (0.01)	3.57E-05	0.05	not tested	not tested	Open Sea	within gene body
cg15988812	chr19: 33889481	<i>PEPD</i>	0.026 (0.006)	3.57E-05	0.05	no	no	North Shelf	within gene body
cg24996724	chr16: 2286426	<i>DNASE1L2</i>	-0.028 (0.006)	3.56E-05	0.05	not tested	not tested	South Shore	within 200 bp of TSS
cg00453272	chr10: 76574026	NA	0.017 (0.004)	3.63E-05	0.05	no	no	South Shore	
cg01362696	chr10: 63348729	NA	-0.031 (0.007)	3.61E-05	0.05	not tested	not tested	Open Sea	
cg07160014	chr11: 47959926	NA	-0.04 (0.009)	3.63E-05	0.05	no	no	Open Sea	
cg09352336	chr6: 3410628	<i>SLC22A23</i>	0.019 (0.004)	3.63E-05	0.05	not tested	not tested	Open Sea	5'UTR
cg10493330	chr5: 179709813	<i>MAPK9</i>	0.015 (0.003)	3.63E-05	0.05	no	no	Open Sea	5'UTR
cg14456982	chr17: 17074142	<i>MPRIP</i>	0.016 (0.004)	3.62E-05	0.05	not tested	not tested	Open Sea	within gene body
cg16840609	chr15: 51397257	<i>TNFAIP8L3</i>	-0.034 (0.008)	3.63E-05	0.05	not tested	not tested	Open Sea	within 1st exon
cg24130603	chr1: 161062428	NA	0.009 (0.002)	3.58E-05	0.05	not tested	not tested	Open Sea	
cg24430703	chr7: 55621681	<i>VOPP1</i>	0.021 (0.005)	3.62E-05	0.05	no	no	Open Sea	within gene body

cg27253783	chr10: 14338581	<i>FRMD4A</i>	0.007 (0.002)	3.61E-05	0.05	not tested	not tested	Open Sea	within gene body
cg11539188	chr10: 3170957	<i>PFKP</i>	0.023 (0.005)	3.64E-05	0.05	not tested	not tested	Open Sea	within gene body
cg12278739	chr11: 68795647	NA	-0.028 (0.006)	3.65E-05	0.05	not tested	not tested	Open Sea	
cg00885708	chr5: 139167076	NA	-0.025 (0.006)	3.69E-05	0.05	no	no	North Shore	
cg06030722	chr6: 127568996	NA	0.01 (0.002)	3.69E-05	0.05	not tested	not tested	Open Sea	
cg11682700	chr3: 114477956	<i>ZBTB20</i>	0.013 (0.003)	3.68E-05	0.05	not tested	not tested	Open Sea	within 1st exon
cg06680529	chr17: 79920755	NA	0.027 (0.006)	3.72E-05	0.05	no	no	Open Sea	in CpG Island
cg04422752	chr10: 102028175	<i>CWF19L1</i>	0.011 (0.002)	3.74E-05	0.05	not tested	not tested	South Shore	within 1500 bp of TSS
cg13705180	chr7: 31978680	<i>PDE1C</i>	0.012 (0.003)	3.74E-05	0.05	not tested	not tested	Open Sea	within gene body
cg07771893	chr16: 27188676	NA	0.015 (0.003)	3.77E-05	0.05	not tested	not tested	Open Sea	
cg18548615	chr17: 32295722	<i>ASIC2</i>	-0.013 (0.003)	3.78E-05	0.05	not tested	not tested	Open Sea	within gene body
cg20779373	chr1: 37428969	<i>GRIK3</i>	-0.035 (0.008)	3.77E-05	0.05	no	no	Open Sea	within gene body
cg25133753	chr20: 44299726	<i>WFDC11</i>	-0.039 (0.009)	3.78E-05	0.05	no	no	Open Sea	within 1500 bp of TSS
cg00367499	chr5: 170634447	<i>RANBP17</i>	0.062 (0.014)	3.81E-05	0.05	not tested	not tested	Open Sea	within gene body
cg01479664	chr16: 58016655	<i>TEPP</i>	0.036 (0.008)	3.81E-05	0.05	no	no	Open Sea	within gene body
cg24409539	chr2: 114034595	<i>PAX8</i>	-0.03 (0.007)	3.81E-05	0.05	no	no	Open Sea	in CpG Island
cg23291484	chr3: 150067838	NA	0.015 (0.003)	3.84E-05	0.05	not tested	not tested	Open Sea	
cg00244312	chr2: 131622518	NA	-0.025 (0.006)	3.86E-05	0.05	not tested	not tested	Open Sea	
cg01447564	chr5: 131335786	<i>ACSL6</i>	-0.042 (0.009)	3.88E-05	0.05	not tested	not tested	Open Sea	within gene body
cg12660171	chr17: 2026359	<i>SMG6</i>	-0.029 (0.007)	3.88E-05	0.05	not tested	not tested	Open Sea	within gene body
cg17258765	chr1: 25202617	NA	0.024 (0.005)	3.86E-05	0.05	not tested	not tested	Open Sea	
cg23978004	chr4: 142144530	<i>ZNF330</i>	0.017 (0.004)	3.88E-05	0.05	no	no	South Shelf	within gene body
cg09012071	chr19: 2171984	<i>DOT1L</i>	-0.027 (0.006)	3.93E-05	0.05	not tested	not tested	Open Sea	within gene body
cg13698574	chr2: 106364714	<i>NCK2</i>	-0.033 (0.008)	3.91E-05	0.05	not tested	not tested	South Shelf	5'UTR
cg14637909	chr10: 103618712	<i>C10orf76</i>	-0.04 (0.009)	3.91E-05	0.05	not tested	not tested	Open Sea	within gene body
cg16294620	chr20: 13280181	<i>ISM1</i>	0.021 (0.005)	3.91E-05	0.05	no	no	South Shore	3'UTR
cg26060224	chr1: 173604924	<i>ANKRD45</i>	0.031 (0.007)	3.92E-05	0.05	not tested	not tested	Open Sea	within gene body
cg26336118	chr1: 97303097	NA	0.008 (0.002)	3.89E-05	0.05	no	no	Open Sea	



cg27010208	chr11: 93263413	<i>SMCO4</i>	-0.03 (0.007)	3.91E-05	0.05	not tested	not tested	Open Sea	5'UTR
cg12434712	chr4: 40005867	NA	0.024 (0.006)	3.94E-05	0.05	not tested	not tested	Open Sea	
cg02998837	chr3: 168619603	<i>LOC100507661</i>	-0.024 (0.006)	4.01E-05	0.05	not tested	not tested	Open Sea	within 200 bp of TSS
cg10217365	chr19: 12890523	NA	-0.031 (0.007)	4.04E-05	0.05	not tested	not tested	South Shore	
cg10473700	chr11: 62359899	<i>TUT1</i>	-0.03 (0.007)	3.98E-05	0.05	not tested	not tested	South Shore	within 1500 bp of TSS
cg11485152	chr3: 3171664	<i>TRNT1</i>	-0.034 (0.008)	3.99E-05	0.05	no	no	South Shelf	within gene body
cg13977520	chr2: 158543191	NA	-0.032 (0.007)	3.98E-05	0.05	not tested	not tested	Open Sea	
cg14200834	chr19: 4278055	<i>SHD</i>	-0.029 (0.007)	3.97E-05	0.05	yes	no	North Shore	within 1500 bp of TSS
cg16521773	chr11: 865988	<i>TSPAN4</i>	0.026 (0.006)	4.01E-05	0.05	no	no	Open Sea	within gene body
cg17178175	chr2: 178109973	<i>NFE2L2</i>	-0.048 (0.011)	4.03E-05	0.05	no	no	Open Sea	within gene body
cg17540831	chr19: 4535992	<i>PLIN5</i>	0.026 (0.006)	4.03E-05	0.05	not tested	not tested	South Shore	within 1500 bp of TSS
cg17754042	chr4: 2338980	<i>ZFYVE28</i>	0.022 (0.005)	3.99E-05	0.05	no	no	North Shelf	within gene body
cg18781031	chr5: 127598507	<i>FBN2</i>	-0.039 (0.009)	3.97E-05	0.05	no	no	Open Sea	within gene body
cg20389995	chr21: 44462317	NA	0.026 (0.006)	4.01E-05	0.05	not tested	not tested	Open Sea	
cg22503060	chr12: 92368774	NA	0.013 (0.003)	3.98E-05	0.05	no	no	Open Sea	
cg22999603	chr11: 119537405	<i>PVRL1</i>	-0.031 (0.007)	3.97E-05	0.05	no	no	South Shore	within gene body
cg24208718	chr1: 212629727	NA	-0.047 (0.011)	4.02E-05	0.05	not tested	not tested	Open Sea	
cg00238899	chr10: 112046866	<i>MXI1</i>	0.013 (0.003)	4.05E-05	0.05	no	no	Open Sea	3'UTR
cg25463683	chr1: 55542596	<i>USP24</i>	-0.02 (0.005)	4.06E-05	0.05	not tested	not tested	Open Sea	within gene body
cg02172658	chr11: 2440093	<i>TRPM5</i>	0.035 (0.008)	4.20E-05	0.05	not tested	not tested	North Shore	within gene body
cg02257445	chr17: 14117857	NA	-0.045 (0.01)	4.12E-05	0.05	not tested	not tested	Open Sea	
cg02862505	chr12: 114939167	NA	0.011 (0.003)	4.14E-05	0.05	no	no	Open Sea	
cg03048947	chr1: 225611366	<i>LBR</i>	-0.045 (0.01)	4.17E-05	0.05	no	no	North Shelf	within gene body
cg04245616	chr15: 59543693	<i>MYO1E</i>	-0.072 (0.017)	4.20E-05	0.05	not tested	not tested	Open Sea	within gene body
cg04399598	chr21: 43956068	<i>SLC37A1</i>	-0.034 (0.008)	4.11E-05	0.05	not tested	not tested	Open Sea	within gene body
cg05075015	chr2: 216317679	<i>LOC102724849</i>	-0.021 (0.005)	4.18E-05	0.05	not tested	not tested	Open Sea	within 1500 bp of TSS

cg05875486	chr11: 655245	<i>DEAF1</i>	0.017 (0.004)	4.17E-05	0.05	not tested	not tested	Open Sea	within gene body
cg06820907	chr2: 242122206	<i>PPP1R7</i>	-0.002 (0)	4.15E-05	0.05	no	no	Open Sea	within gene body
cg08690174	chr6: 123959721	<i>TRDN</i>	-0.046 (0.011)	4.18E-05	0.05	not tested	not tested	Open Sea	within 1500 bp of TSS
cg11014079	chr7: 149517605	<i>SSPO</i>	-0.02 (0.005)	4.15E-05	0.05	no	no	Open Sea	within gene body
cg18024141	chr6: 152232729	<i>ESR1</i>	-0.029 (0.007)	4.11E-05	0.05	not tested	not tested	Open Sea	within gene body
cg18049487	chr19: 40709597	<i>MAP3K10</i>	0.017 (0.004)	4.14E-05	0.05	not tested	not tested	North Shelf	within gene body
cg19361399	chr2: 67405276	<i>LOC102800447</i>	0.035 (0.008)	4.12E-05	0.05	not tested	not tested	Open Sea	within gene body
cg21995472	chr12: 85271218	<i>SLC6A15</i>	-0.047 (0.011)	4.13E-05	0.05	not tested	not tested	Open Sea	within gene body
cg22393541	chr12: 11081043	<i>PRH2</i>	0.01 (0.002)	4.08E-05	0.05	not tested	not tested	Open Sea	within 1500 bp of TSS
cg24948374	chr20: 62869833	<i>MYT1</i>	-0.024 (0.006)	4.21E-05	0.05	not tested	not tested	Open Sea	within gene body
cg25221207	chr11: 119555633	<i>PVRL1</i>	-0.026 (0.006)	4.10E-05	0.05	no	no	Open Sea	within gene body
cg25506287	chr6: 26247955	<i>HIST1H4G</i>	0.009 (0.002)	4.14E-05	0.05	not tested	not tested	South Shore	within 1500 bp of TSS
cg26351916	chr17: 78084228	<i>GAA</i>	0.024 (0.005)	4.17E-05	0.05	no	no	South Shore	within gene body
cg27209994	chr18: 51750371	<i>MBD2</i>	0.007 (0.002)	4.09E-05	0.05	no	no	North Shore	within gene body
cg27399052	chr1: 1293868	<i>MXRA8</i>	-0.025 (0.006)	4.20E-05	0.05	no	no	South Shelf in CpG Island	within 1st exon
cg20478080	chr22: 45133246	<i>PRR5</i>	0.023 (0.005)	4.22E-05	0.05	no	no	Open Sea	3'UTR within gene body
cg05214676	chr4: 141005085	<i>MAML3</i>	0.031 (0.007)	4.25E-05	0.05	no	no	Open Sea	within gene body
cg00693782	chr11: 11097882	NA	-0.041 (0.009)	4.29E-05	0.05	not tested	not tested	Open Sea	
cg26686150	chr12: 93637466	NA	-0.026 (0.006)	4.29E-05	0.05	no	no	Open Sea	
cg06177446	chr20: 1093802	<i>PSMF1</i>	0.02 (0.005)	4.31E-05	0.05	no	no	Open Sea	within 200 bp of TSS
cg04394031	chr11: 65416901	<i>SIPA1</i>	0.025 (0.006)	4.33E-05	0.05	no	no	South Shore	within gene body
cg14540181	chr7: 7330669	NA	0.029 (0.007)	4.33E-05	0.05	not tested	not tested	Open Sea	
cg17463863	chr3: 139106943	<i>COPB2</i>	0.022 (0.005)	4.32E-05	0.05	not tested	not tested	North Shore	within gene body
cg18815657	chr5: 74130379	<i>FAM169A</i>	-0.03 (0.007)	4.34E-05	0.05	not tested	not tested	Open Sea	within gene body
cg23718496	chr19: 47875594	<i>DHX34</i>	0.018 (0.004)	4.38E-05	0.05	not tested	not tested	Open Sea	within gene body

cg17064521	chr15: 45740423	NA	-0.023 (0.005)	4.40E-05	0.05	not tested	not tested	Open Sea	
cg01047262	chr8: 38007025	<i>STAR</i>	-0.017 (0.004)	4.47E-05	0.05	not tested	not tested	Open Sea	within gene
cg01276573	chr17: 28672068	NA	-0.027 (0.006)	4.45E-05	0.05	not tested	not tested	Open Sea	body
cg02649474	chr16: 30673103	<i>FBRS</i>	0.02 (0.005)	4.48E-05	0.05	not tested	not tested	South Shore	within gene
cg06039201	chr3: 50737816	<i>DOCK3</i>	0.013 (0.003)	4.45E-05	0.05	not tested	not tested	Open Sea	body
cg06540015	chr1: 32203668	<i>ADGRB2</i>	0.024 (0.006)	4.42E-05	0.05	not tested	not tested	Open Sea	within gene
cg07092838	chr17: 72248179	<i>TTYH2</i>	0.024 (0.005)	4.48E-05	0.05	not tested	not tested	Open Sea	body
cg13176608	chr1: 204542634	NA	0.027 (0.006)	4.46E-05	0.05	not tested	not tested	Open Sea	
cg19989663	chr7: 115981565	NA	-0.056 (0.013)	4.46E-05	0.05	not tested	not tested	Open Sea	
cg20181240	chr1: 4029800	NA	-0.049 (0.011)	4.44E-05	0.05	not tested	not tested	Open Sea	
cg20335206	chr12: 120802252	<i>MSI1</i>	0.021 (0.005)	4.45E-05	0.05	no	no	North Shelf	within gene body

<sup>a</sup> Genomic location is according to genome build GRCh37/hg19

<sup>b</sup> Effect estimates represent the proportion of methylation difference at follow-up compared to baseline, adjusted for batch, cell type estimates, Hispanic ethnicity, estimated smoking pack-years, and a random intercept for individual to account for the repeated sampling design.

<sup>c</sup> Was this CpG site statistically significantly different when comparing current (or former) adult smokers to adults who never smoked? Comparing from the meta-analysis of ~16,000 adults published in Joehanes et al. 2016 *Circ Cardiovas Genetics* 9(5):436-447. Joehanes et al. used the 450K; 'not tested' sites were not included on that version of the Infinium array.

<sup>d</sup> Location of CpG site relative to a CpG Island

<sup>e</sup> Location of CpG site relative to nearest gene according to annotations from UCSC RefGene

**Supplemental Table S2. Difference in DNA methylation between baseline and follow-up at CpG sites Previously associated with firefighting**

Probe ID <sup>a</sup>	Genomic Location <sup>b</sup>	Gene Name	Estimate (SE) <sup>c</sup>	p-value
cg15304928	chr1: 201123562	<i>TMEM9</i>	-0.001 (0.002)	0.632
cg00287370	chr1: 234736092	NA	0.009 (0.004)	<b>0.009</b>
cg02932780	chr6: 31762353	<i>VAR5</i>	-0.005 (0.007)	0.541
cg09544149	chr10: 80588828	NA	-0.048 (0.016)	<b>0.004</b>
cg05236728	chr12: 47609513	<i>PCED1B-AS1</i>	0.001 (0.001)	0.309
cg03177084	chr17: 40985069	<i>PSME3</i>	0.002 (0.003)	0.535
cg22433210	chr17: 43662623	NA	-0.001 (0)	<b>0.031</b>
cg13753209	chr17: 57696993	<i>CLTC</i>	0 (0)	0.718
cg22280238	chr17: 79251323	<i>SLC38A10</i>	-0.001 (0.001)	0.197
cg07897354	chr18: 12657909	<i>SPIRE1</i>	0 (0)	0.280
cg20821958	chr19: 48614116	<i>PLA2G4C</i>	0.002 (0.001)	<b>0.007</b>
cg12253469	chr22: 37420454	<i>MPST</i>	-0.008 (0.015)	0.575
cg24034992	chrX: 67719066	<i>YIPF6</i>	-0.001 (0.006)	0.817

<sup>a</sup> Only CpG sites that differed when comparing new recruits and incumbent firefighters or associated with years in the service are included in this table, from Zhou et al. 2019

<sup>b</sup> Genomic location is according to genome build GRCh37/hg19

<sup>c</sup> Effect estimates represent the proportion of methylation difference at follow-up compared to baseline, adjusted for batch, cell type estimates, Hispanic ethnicity, estimated smoking pack-years, and a random intercept for individual to account for the repeated sampling.

NA means the CpG site is not within a gene or within a known feature (e.g. promoter) of a specific gene.

**Supplemental Table S3. Enriched gene sets annotated to disease and disease-related functions in IPA among differentially methylated genes comparing baseline to follow-up ( $q < 0.05$ )**

<b>Broader Category of Disease</b>	<b>Gene-Set (Disease or Functional Annotation)</b>	<b>q-value for enrichment</b>	<b># Differentially Methylated Genes in the gene-set</b>
Cancer,Cell Cycle,Organismal Injury and Abnormalities	Interphase of cancer cells	0.030	4
	Arrest in interphase of cancer cells	0.035	3
	Arrest in G2 phase of cancer cells	0.044	2
Cancer,Dermatological Diseases and Conditions,Organismal Injury and Abnormalities	Skin cancer	0.048	242
Cancer,Endocrine System Disorders,Gastrointestinal Disease,Organismal Injury and Abnormalities	Pancreatic tumor	0.020	100
	Pancreatic cancer	0.035	88
	Pancreatic carcinoma	0.042	84
	Pancreatic adenocarcinoma	0.042	80
	Pancreatic ductal adenocarcinoma	0.044	78
Cancer,Gastrointestinal Disease,Organismal Injury and Abnormalities	Large intestine adenocarcinoma	0.001	277
	Large intestine neoplasm	0.001	283
	Malignant neoplasm of large intestine	0.001	282
	Colon tumor	0.001	178
	Gastrointestinal adenocarcinoma	0.001	280
	Stomach tumor	0.001	141
	Gastrointestinal carcinoma	0.001	288
	Development of digestive organ tumor	0.001	215
	Gastro-esophageal carcinoma	0.001	143
	Gastroesophageal cancer	0.001	146
	Gastric cancer	0.001	139
	Colon cancer	0.001	175
	Colorectal adenocarcinoma	0.001	173
	Gastric carcinoma	0.001	135

	Upper gastrointestinal tract tumor	0.001	166
	Non-colon gastrointestinal cancer	0.001	172
	Gastrointestinal tract cancer	0.002	291
	Colon adenocarcinoma	0.002	166
	Colorectal carcinoma	0.002	174
	Upper gastrointestinal carcinoma	0.002	161
	Upper gastrointestinal tract cancer	0.002	164
	Colon carcinoma	0.003	167
	Colorectal tumor	0.005	187
	Colorectal cancer	0.008	184
	Pancreatobiliary tumor	0.020	113
	Digestive system cancer	0.021	302
	Mismatch repair deficient colorectal adenocarcinoma	0.035	4
	Metastatic BRAF V600E mutation positive colon cancer	0.035	3
	Metastatic BRAF V600E mutation positive rectal cancer	0.035	3
	Advanced BRAF V600E mutation positive colon cancer	0.035	3
	Advanced BRAF V600E mutation positive rectal cancer	0.035	3
	Replication error repair positive colorectal tumor	0.037	4
Cancer,Gastrointestinal Disease,Organismal Injury and Abnormalities,Tumor Morphology	Metastatic progressive colorectal cancer	0.020	4
Cancer,Hematological Disease,Immunological Disease,Organismal Injury and Abnormalities	Precursor B-cell acute lymphoblastic leukemia	0.019	31
	Acute lymphoblastic leukemia	0.020	36
	B-cell leukemia	0.036	35
Cancer,Neurological Disease,Organismal Injury and Abnormalities	Central nervous system cancer	0.001	228
	Nervous system neoplasm	0.001	232
	Central nervous system solid tumor	0.001	230
	Brain glioma	0.001	221

	Glioma cancer	0.001	223
	Brain tumor	0.001	222
	Glioma	0.001	225
	Brain cancer	0.001	107
	Gliomatosis cerebri	0.005	99
	Brain astrocytoma	0.014	167
	High grade astrocytoma	0.015	172
	Grade 1-4 astrocytoma	0.016	167
	Grade 3-4 glioma	0.017	185
	Grade 3-4 glioma cancer	0.020	184
	Grade 4 high grade glioma	0.020	165
	Grade 4 malignant glioma	0.020	165
	Grade 4 astrocytoma	0.020	165
	Tumorigenesis of glioblastoma	0.022	2
	Meningioma	0.023	17
Cancer,Organismal Injury and Abnormalities	Breast or colorectal cancer	0.001	220
	Melanoma	0.003	264
	Malignant connective or soft tissue neoplasm	0.007	252
	Abdominal adenocarcinoma	0.007	304
	Formation of solid tumor	0.007	302
	Connective or soft tissue tumor	0.011	253
	Malignant soft tissue neoplasm	0.011	249
	Development of carcinoma	0.012	266
	Cancer of head	0.013	124
	Tumorigenesis of epithelial neoplasm	0.013	267
	Frequency of tumor	0.013	268
	Breast or pancreatic cancer	0.015	170
	Head and neck tumor	0.017	306
	Adenocarcinoma	0.017	306
	Non-hematological solid tumor	0.017	336
	Incidence of tumor	0.019	271
	Head and neck squamous cell carcinoma	0.020	99

	Malignant solid organ tumor	0.021	247
	Nonhematologic malignant neoplasm	0.029	335
	Head and neck cancer	0.032	289
	Extraadrenal retroperitoneal tumor	0.035	123
	Head and neck carcinoma	0.037	280
	Malignant neoplasm of retroperitoneum	0.045	113
Cancer,Organismal Injury and Abnormalities,Reproductive System Disease	Breast or ovarian carcinoma	0.028	117
	Breast carcinoma	0.034	84
	Breast cancer	0.044	99
	Mammary tumor	0.049	100
Cancer,Organismal Injury and Abnormalities,Respiratory Disease	Stage IIIB primary non-squamous non-small cell lung carcinoma	0.044	2
	Stage IV primary non-squamous non-small cell lung carcinoma	0.044	2
	Primary EGFR mutation positive non-small cell lung carcinoma	0.044	2
	Stage IV EGFR activating mutation positive EGFR T790M mutation negative nonsquamous non-small cell lung carcinoma	0.044	2
	EGFR T790M mutation negative EGFR exon 20 insertion mutation negative non-small cell lung carcinoma	0.044	2
Cancer,Organismal Injury and Abnormalities,Tumor Morphology	Regression of tumor	0.035	3
Cardiovascular Disease,Cardiovascular System Development and Function,Organ Morphology,Organismal Development,Organismal Injury and Abnormalities,Skeletal and Muscular Disorders	Dilated cardiomyopathy	0.042	13
Cardiovascular System Development and Function,Cellular Development,Cellular Growth and Proliferation	Colony formation of endothelial cell lines	0.044	2
Cardiovascular System Development and Function,Organ Development,Organ Morphology	Contraction of heart	0.020	7
Cell Cycle	Arrest in interphase of tumor cell lines	0.017	19
	Arrest in interphase	0.038	20
	Arrest in G1 phase of tumor cell lines	0.043	13



Cell-To-Cell Signaling and Interaction	Activation of cells	0.007	25
Cell-To-Cell Signaling and Interaction,Hematological System Development and Function	Activation of blood cells	0.020	19
Cellular Development	Epithelial-mesenchymal transition of tumor cell lines	0.045	10
Cellular Development,Cellular Growth and Proliferation,Hematological System Development and Function,Hematopoiesis,Tissue Development	Development of hematopoietic progenitor cells	0.017	11
Cellular Movement	Cell movement of tumor cell lines	0.026	46
	Migration of tumor cell lines	0.029	41
	Migration of cells	0.042	57
	Homing of tumor cell lines	0.049	9
Cellular Movement,Nervous System Development and Function	Migration of neuroglia	0.017	3
Connective Tissue Disorders,Inflammatory Disease,Inflammatory Response,Organismal Injury and Abnormalities,Skeletal and Muscular Disorders	Inflammation of joint	0.044	39
Dermatological Diseases and Conditions,Organismal Injury and Abnormalities	Skin lesion	0.034	244
Developmental Disorder,Hereditary Disorder,Neurological Disease,Organismal Injury and Abnormalities	CHARGE syndrome	0.029	3
Gene Expression	Activation of DNA endogenous promoter	0.001	41
	Transcription	0.002	66
	Transcription of RNA	0.003	59
	Transcription of DNA	0.007	48
	Expression of RNA	0.014	65
	Synthesis of rRNA	0.035	3
Hematological System Development and Function,Hematopoiesis	Development of hematopoietic system	0.013	12
Neurological Disease,Organismal Injury and Abnormalities	Cerebral disorder	0.011	106

Supplemental Table S4. Associations between Proxies of Cumulative Fireground Exposures and DNA Methylation (q&lt;0.05)

Genomic Location <sup>a</sup>	Gene Name	Fire-Hours, All Fires		Fire-Runs, All Fires		Fire-Hours, Structure Fires		Fire-Runs, Structure Fires	
		Estimate (SE) <sup>b</sup>	q-value	Estimate (SE) <sup>b</sup>	q-value	Estimate (SE) <sup>b</sup>	q-value	Estimate (SE) <sup>b</sup>	q-value
chr1:1293868	<i>MXRA8</i>	-0.0139 (0.0066)	0.14	-0.0164 (0.0057)	0.04	-0.0097 (0.0072)	0.37	-0.0134 (0.0077)	0.19
chr1:1912135	<i>CFAP74</i>	0.0174 (0.0056)	0.05	0.016 (0.0049)	0.02	0.0164 (0.0063)	0.12	0.0171 (0.0068)	0.08
chr1:2027575	<i>PRKCZ</i>	0.0144 (0.0052)	0.07	0.0152 (0.0045)	0.02	0.0111 (0.0058)	0.23	0.0168 (0.0061)	0.06
chr1:8797440	<i>RERE</i>	-0.0312 (0.0107)	0.07	-0.0291 (0.0095)	0.04	-0.0315 (0.0117)	0.11	-0.0357 (0.0125)	0.05
chr1:11795976	<i>AGTRAP</i>	-0.0234 (0.0084)	0.07	-0.0209 (0.0074)	0.04	-0.019 (0.0093)	0.22	-0.0239 (0.0099)	0.09
chr1:27874526	<i>AHDC1</i>	0.0152 (0.0063)	0.11	0.0154 (0.0054)	0.04	0.011 (0.007)	0.31	0.0147 (0.0074)	0.14
chr1:32670695	<i>IQCC</i>	0.0334 (0.007)	0.01	0.0322 (0.0061)	0.00	0.0335 (0.0078)	0.04	0.0397 (0.0083)	0.00
chr1:45254092	<i>BEST4</i>	-0.0268 (0.0088)	0.06	-0.0277 (0.0076)	0.02	-0.0218 (0.01)	0.19	-0.0234 (0.0108)	0.12
chr1:97303097	NA	0.0054 (0.0021)	0.10	0.0055 (0.0018)	0.04	0.0036 (0.0024)	0.31	0.0053 (0.0025)	0.13
chr1:109843435	<i>MYBPHL</i>	-0.0245 (0.0078)	0.05	-0.0252 (0.0068)	0.02	-0.0256 (0.0086)	0.09	-0.0374 (0.0089)	0.01
chr1:150668227	<i>GOLPH3L</i>	-0.0257 (0.0097)	0.09	-0.0254 (0.0085)	0.04	-0.0262 (0.0107)	0.14	-0.0323 (0.0113)	0.05
chr1:156865043	<i>PEAR1</i>	-0.0126 (0.0079)	0.23	-0.01 (0.0071)	0.24	-0.02 (0.0084)	0.15	-0.0264 (0.009)	0.05
chr1:185227307	<i>SWT1</i>	0.0135 (0.006)	0.13	0.0144 (0.0052)	0.05	0.0091 (0.0067)	0.36	0.012 (0.0071)	0.20
chr1:192736213	NA	-0.0096 (0.004)	0.11	-0.0102 (0.0034)	0.04	-0.0086 (0.0044)	0.22	-0.0106 (0.0047)	0.11
chr1:204542634	NA	0.0213 (0.007)	0.05	0.021 (0.006)	0.02	0.0154 (0.0079)	0.22	0.0156 (0.0085)	0.17
chr1:206971195	<i>IL19</i>	-0.021 (0.0097)	0.13	-0.0249 (0.0084)	0.04	-0.0156 (0.0108)	0.34	-0.0263 (0.0114)	0.10
chr1:228112951	<i>WNT9A</i>	0.0202 (0.0081)	0.10	0.0248 (0.0068)	0.02	0.0102 (0.0091)	0.44	0.0187 (0.0096)	0.15
chr1:235931377	<i>LYST</i>	-0.0429 (0.0119)	0.04	-0.0414 (0.0103)	0.01	-0.0406 (0.0133)	0.09	-0.0492 (0.014)	0.03
chr2:54756403	<i>RPL23AP32</i>	0.009 (0.0027)	0.05	0.0091 (0.0024)	0.02	0.0057 (0.0031)	0.25	0.0053 (0.0034)	0.24
chr2:70792316	NA	0.0094 (0.0042)	0.13	0.0102 (0.0037)	0.04	0.0051 (0.0048)	0.45	0.01 (0.005)	0.14
chr2:109941286	<i>SH3RF3</i>	0.0048 (0.0023)	0.14	0.0036 (0.002)	0.16	0.007 (0.0024)	0.10	0.0082 (0.0026)	0.04
chr2:114034595	<i>PAX8</i>	-0.0234 (0.0076)	0.05	-0.0213 (0.0067)	0.03	-0.0178 (0.0084)	0.20	-0.0187 (0.0092)	0.13

chr2:178109973	<i>NFE2L2</i>	-0.0242 (0.0126)	0.17	-0.0323 (0.0109)	0.04	-0.0121 (0.0139)	0.55	-0.0248 (0.0149)	0.20
chr2:201593511	<i>AOX2P</i>	-0.0196 (0.0066)	0.06	-0.0174 (0.0058)	0.04	-0.0146 (0.0075)	0.23	-0.0177 (0.0081)	0.12
chr2:240044446	<i>HDAC4</i>	0.0149 (0.006)	0.10	0.0139 (0.0052)	0.05	0.0181 (0.0065)	0.10	0.0201 (0.007)	0.05
chr2:241990667	<i>SNED1</i>	0.0174 (0.0055)	0.05	0.0177 (0.0047)	0.02	0.0142 (0.0062)	0.17	0.0166 (0.0066)	0.08
chr3:9811912	<i>CAMK1</i>	-0.0215 (0.0071)	0.06	-0.0173 (0.0065)	0.06	-0.0259 (0.0075)	0.07	-0.027 (0.0081)	0.04
chr3:31145476	NA	-0.0087 (0.0046)	0.17	-0.0068 (0.0041)	0.19	-0.0136 (0.0049)	0.10	-0.0156 (0.0053)	0.05
chr3:46009762	<i>FYCO1</i>	0.0143 (0.0046)	0.05	0.0134 (0.004)	0.02	0.0151 (0.0051)	0.09	0.0178 (0.0054)	0.04
chr3:49966773	<i>MON1A</i>	0.006 (0.0023)	0.10	0.0056 (0.002)	0.05	0.0044 (0.0026)	0.27	0.005 (0.0028)	0.18
chr3:52008487	<i>ABHD14B</i>	-0.0111 (0.0078)	0.27	-0.0123 (0.0068)	0.16	-0.0174 (0.0085)	0.21	-0.0265 (0.0089)	0.05
chr3:58367583	<i>PXK</i>	0.0256 (0.0148)	0.20	0.0271 (0.0129)	0.10	0.0378 (0.016)	0.15	0.0509 (0.0168)	0.04
chr3:89097455	NA	-0.0215 (0.0073)	0.06	-0.0189 (0.0064)	0.04	-0.0223 (0.008)	0.10	-0.0284 (0.0085)	0.04
chr3:109746788	NA	-0.026 (0.0098)	0.09	-0.0228 (0.0087)	0.06	-0.0302 (0.0106)	0.10	-0.0373 (0.0114)	0.04
chr3:132450221	<i>NPHP3-AS1</i>	-0.0278 (0.0125)	0.13	-0.0275 (0.011)	0.07	-0.0294 (0.0137)	0.20	-0.0415 (0.0143)	0.05
chr4:65749341	NA	-0.0556 (0.016)	0.04	-0.0498 (0.0141)	0.02	-0.0634 (0.0175)	0.07	-0.0582 (0.0192)	0.04
chr4:72897317	<i>NPFFR2</i>	0.0168 (0.0052)	0.05	0.0174 (0.0044)	0.01	0.0142 (0.0058)	0.14	0.0186 (0.0062)	0.04
chr4:73969865	<i>ANKRD17</i>	0.0116 (0.0039)	0.06	0.0098 (0.0035)	0.04	0.0105 (0.0044)	0.15	0.0099 (0.0047)	0.13
chr4:76440740	<i>RCHY1</i>	-0.0381 (0.0158)	0.12	-0.0386 (0.0139)	0.05	-0.0447 (0.0172)	0.12	-0.056 (0.0183)	0.04
chr4:111533823	NA	-0.0214 (0.0079)	0.08	-0.0199 (0.0071)	0.04	-0.0195 (0.0087)	0.18	-0.0242 (0.0093)	0.08
chr5:2758088	NA	-0.0138 (0.0073)	0.17	-0.0153 (0.0063)	0.07	-0.0142 (0.008)	0.25	-0.0243 (0.0084)	0.05
chr5:38427885	<i>EGFLAM</i>	-0.0361 (0.0129)	0.07	-0.0333 (0.0114)	0.04	-0.047 (0.0136)	0.07	-0.0602 (0.014)	0.01
chr5:60622671	NA	0.0245 (0.0076)	0.05	0.0261 (0.0066)	0.01	0.0151 (0.0087)	0.26	0.0192 (0.0093)	0.13
chr5:71764958	<i>ZNF366</i>	-0.0366 (0.0103)	0.04	-0.0364 (0.009)	0.01	-0.035 (0.0115)	0.09	-0.0472 (0.0121)	0.02
chr5:88875631	NA	-0.0337 (0.0095)	0.04	-0.0306 (0.0083)	0.02	-0.0325 (0.0106)	0.09	-0.0392 (0.0113)	0.03
chr5:117897957	<i>HRAT56</i>	0.0122 (0.0033)	0.04	0.013 (0.0028)	0.00	0.0059 (0.0039)	0.31	0.0096 (0.0041)	0.10
chr5:142422241	<i>ARHGAP26</i>	0.0075 (0.003)	0.10	0.0085 (0.0025)	0.02	0.0024 (0.0034)	0.61	0.0044 (0.0036)	0.34
chr5:153211415	NA	-0.0231 (0.0099)	0.12	-0.0247 (0.0086)	0.04	-0.0249 (0.0108)	0.17	-0.0354 (0.0115)	0.04
chr5:179709813	<i>MAPK9</i>	0.0073 (0.004)	0.18	0.0075 (0.0035)	0.10	0.0088 (0.0044)	0.22	0.0131 (0.0046)	0.05
chr6:13007033	<i>PHACTR1</i>	-0.0212 (0.0124)	0.21	-0.0186 (0.0109)	0.17	-0.0284 (0.0135)	0.20	-0.0417 (0.0141)	0.05

chr6:13053520	<i>PHACTR1</i>	-0.0419 (0.0126)	0.05	-0.0412 (0.011)	0.02	-0.0379 (0.0141)	0.11	-0.0482 (0.0149)	0.04
chr6:30159309	<i>TRIM26</i>	0.0075 (0.0032)	0.12	0.0095 (0.0027)	0.02	0.0015 (0.0036)	0.77	0.0052 (0.0038)	0.29
chr6:46380623	<i>RCAN2</i>	-0.0267 (0.0104)	0.10	-0.0266 (0.0092)	0.04	-0.0178 (0.0115)	0.31	-0.0225 (0.0124)	0.17
chr6:101880078	<i>GRIK2</i>	-0.0326 (0.0129)	0.10	-0.0346 (0.0112)	0.04	-0.0308 (0.0143)	0.19	-0.0425 (0.0151)	0.05
chr6:152232729	<i>ESR1</i>	-0.0234 (0.0071)	0.05	-0.0198 (0.0064)	0.04	-0.027 (0.0077)	0.07	-0.0318 (0.0082)	0.02
chr7:2158623	<i>MAD1L1</i>	0.0255 (0.0069)	0.04	0.0272 (0.0059)	0.00	0.0178 (0.008)	0.18	0.0235 (0.0084)	0.06
chr7:2663085	NA	-0.0112 (0.0075)	0.26	-0.0087 (0.0066)	0.27	-0.0219 (0.0079)	0.10	-0.0249 (0.0085)	0.05
chr7:14899040	NA	-0.0306 (0.0145)	0.14	-0.0356 (0.0125)	0.04	-0.0203 (0.0163)	0.40	-0.0375 (0.0171)	0.12
chr7:48127925	<i>UPP1</i>	-0.0155 (0.0075)	0.14	-0.0177 (0.0065)	0.05	-0.0134 (0.0083)	0.29	-0.0166 (0.0089)	0.16
chr7:100282651	<i>GIGYF1</i>	0.0157 (0.0047)	0.05	0.0136 (0.0041)	0.02	0.0149 (0.0052)	0.10	0.0166 (0.0056)	0.04
chr7:150086034	<i>ZNF775</i>	-0.0296 (0.0114)	0.09	-0.0291 (0.01)	0.04	-0.024 (0.0128)	0.24	-0.0343 (0.0135)	0.08
chr8:27114746	<i>STMN4</i>	-0.035 (0.009)	0.04	-0.0327 (0.008)	0.01	-0.032 (0.01)	0.09	-0.0369 (0.011)	0.04
chr8:128512692	NA	0.0067 (0.0032)	0.14	0.008 (0.0028)	0.04	0.002 (0.0036)	0.71	0.0056 (0.0039)	0.26
chr9:5186210	<i>INSL6</i>	0.0093 (0.0037)	0.10	0.0092 (0.0032)	0.04	0.0069 (0.0041)	0.27	0.0079 (0.0044)	0.18
chr9:135852984	<i>GFI1B</i>	-0.0263 (0.0098)	0.08	-0.0245 (0.0086)	0.04	-0.0262 (0.0107)	0.14	-0.0308 (0.0114)	0.07
chr9:140174741	<i>C9orf167</i>	0.023 (0.0072)	0.05	0.0217 (0.0063)	0.02	0.0231 (0.008)	0.10	0.0308 (0.0084)	0.02
chr9:140376822	<i>PNPLA7</i>	-0.02 (0.0072)	0.08	-0.021 (0.0063)	0.02	-0.0167 (0.008)	0.20	-0.0264 (0.0084)	0.04
chr10:14338581	<i>FRMD4A</i>	0.0045 (0.0018)	0.11	0.0044 (0.0016)	0.05	0.0038 (0.0021)	0.25	0.0046 (0.0022)	0.13
chr10:76661092	<i>KAT6B</i>	-0.0353 (0.0094)	0.04	-0.0327 (0.0083)	0.01	-0.0348 (0.0105)	0.07	-0.0378 (0.0113)	0.04
chr10:134211857	<i>PWWP2B</i>	-0.0283 (0.0105)	0.08	-0.0279 (0.0092)	0.04	-0.0182 (0.0118)	0.31	-0.0253 (0.0128)	0.14
chr11:1536810	<i>HCCA2</i>	-0.0178 (0.0112)	0.23	-0.0179 (0.0099)	0.15	-0.0277 (0.012)	0.17	-0.0363 (0.0127)	0.05
chr11:5538958	<i>UBQLNL</i>	-0.033 (0.0095)	0.04	-0.0257 (0.0085)	0.04	-0.0368 (0.0104)	0.07	-0.0348 (0.0114)	0.04
chr11:11866554	<i>USP47</i>	-0.0225 (0.0083)	0.08	-0.0153 (0.0075)	0.11	-0.0345 (0.0087)	0.06	-0.0327 (0.0096)	0.04
chr11:47959926	NA	-0.031 (0.0099)	0.05	-0.0283 (0.0086)	0.02	-0.0285 (0.011)	0.12	-0.0357 (0.0117)	0.04
chr11:62600230	<i>STX5</i>	-0.0249 (0.0089)	0.07	-0.0213 (0.0079)	0.05	-0.0285 (0.0096)	0.10	-0.0349 (0.0102)	0.04
chr11:65378788	<i>MAP3K11</i>	-0.0115 (0.0063)	0.18	-0.011 (0.0055)	0.12	-0.0187 (0.0067)	0.10	-0.0216 (0.0071)	0.04
chr11:68795647	NA	-0.0251 (0.0069)	0.04	-0.0186 (0.0062)	0.04	-0.0253 (0.0076)	0.07	-0.0254 (0.0082)	0.04
chr11:79613887	NA	-0.0266 (0.0096)	0.07	-0.0281 (0.0083)	0.02	-0.027 (0.0106)	0.13	-0.0335 (0.0113)	0.05

chr11:119537405	<i>PVRL1</i>	-0.0185 (0.0082)	0.13	-0.0151 (0.0072)	0.11	-0.0228 (0.0089)	0.13	-0.0288 (0.0094)	0.04
chr12:11081043	<i>PRH2</i>	0.006 (0.0026)	0.13	0.0069 (0.0023) -0.0138 (0.0044)	0.04	0.0057 (0.0029)	0.23	0.0082 (0.0031)	0.07
chr12:42102842	NA	-0.0144 (0.0051)	0.07	-0.0188 (0.0062)	0.03	-0.0141 (0.0056)	0.13	-0.0166 (0.006)	0.06
chr12:52435577	<i>NR4A1</i>	-0.0169 (0.0071)	0.12	-0.0229 (0.0067)	0.04	-0.0184 (0.0077)	0.15	-0.028 (0.0079)	0.03
chr12:54402050	<i>HOXC8</i>	-0.0241 (0.0077)	0.05	-0.0368 (0.012) -0.0159 (0.0056)	0.02	-0.0238 (0.0084)	0.10	-0.0302 (0.009)	0.04
chr12:119621039	<i>HSPB8</i>	-0.0352 (0.0138)	0.10	-0.0159 (0.0047)	0.04	-0.0212 (0.0153)	0.36	-0.0328 (0.0164)	0.14
chr12:120559003	NA	-0.0153 (0.0064)	0.12	-0.0254 (0.0086)	0.04	-0.0141 (0.007)	0.22	-0.02 (0.0075)	0.07
chr12:120802252	<i>MS1</i>	0.0141 (0.0054)	0.09	-0.0137 (0.0067)	0.04	0.0117 (0.0061)	0.23	0.0149 (0.0065)	0.10
chr13:35043968	<i>LINC00457</i>	-0.022 (0.01)	0.13	-0.0494 (0.0147)	0.04	-0.0273 (0.0108)	0.13	-0.047 (0.0109)	0.01
chr13:72778607	NA	-0.0168 (0.0075)	0.13	-0.0563 (0.015) -0.0227 (0.0079)	0.11	-0.0221 (0.0081)	0.10	-0.0247 (0.0087)	0.05
chr14:24858912	NA	-0.0461 (0.0169)	0.08	-0.0157 (0.0058)	0.02	-0.0365 (0.0191)	0.23	-0.0498 (0.0206)	0.09
chr14:63785523	<i>GPHB5</i>	-0.0599 (0.0168)	0.04	-0.0227 (0.0079)	0.02	-0.0665 (0.0176)	0.07	-0.0762 (0.0191)	0.02
chr14:105955879	<i>C14orf80</i>	-0.0205 (0.009)	0.13	-0.0157 (0.0058)	0.04	-0.0179 (0.01)	0.25	-0.0228 (0.0108)	0.13
chr15:45406362	<i>DUOX2</i>	-0.015 (0.0066)	0.13	0.01 (0.0029)	0.05	-0.0134 (0.0073)	0.25	-0.0221 (0.0077)	0.05
chr15:58011290	NA	0.0101 (0.0034)	0.06	0.0102 (0.0042) -0.0195 (0.0068)	0.02	0.0079 (0.0038)	0.20	0.0101 (0.004)	0.08
chr15:68933603	<i>CORO2B</i>	0.0118 (0.0048)	0.11	0.0151 (0.0057) 0.0116 (0.004) -0.0177 (0.0077)	0.08	0.0162 (0.0051)	0.09	0.0173 (0.0055)	0.04
chr16:1386290	<i>BAIAP3</i>	-0.0189 (0.0077)	0.11	0.0136 (0.0047)	0.04	-0.0233 (0.0082)	0.10	-0.0323 (0.0086)	0.02
chr16:1420171	<i>UNKL</i>	0.0137 (0.0054)	0.10	0.0151 (0.0057)	0.04	0.0102 (0.0061)	0.27	0.0117 (0.0065)	0.17
chr16:2086421	<i>SLC9A3R2</i>	0.0159 (0.0064)	0.10	0.0116 (0.004) -0.0177 (0.0077)	0.05	0.0183 (0.007)	0.12	0.0248 (0.0074)	0.04
chr16:28922391	<i>RABEP2</i>	0.0093 (0.0046)	0.16	0.0116 (0.004) -0.0177 (0.0077)	0.04	0.0028 (0.0052)	0.71	0.0095 (0.0055)	0.18
chr16:57984539	<i>CNGB1</i>	-0.0201 (0.0087)	0.13	0.0221 (0.0064)	0.08	-0.0253 (0.0093)	0.11	-0.033 (0.0098)	0.04
chr16:88096588	<i>BANP</i>	0.0194 (0.0075)	0.09	0.0118 (0.0049)	0.02	0.0089 (0.0085)	0.46	0.0157 (0.009)	0.18
chr16:88979098	<i>CBFA2T3</i>	0.0108 (0.0057)	0.17	0.0118 (0.0049)	0.08	0.0113 (0.0063)	0.25	0.0201 (0.0065)	0.04
chr16:89922539	<i>SPIRE2</i>	0.0186 (0.006)	0.05	0.015 (0.0053)	0.04	0.0202 (0.0065)	0.09	0.0188 (0.0071)	0.07
chr17:1059336	<i>ABR</i>	0.0103 (0.0051)	0.15	0.0099 (0.0044)	0.09	0.015 (0.0054)	0.10	0.0187 (0.0058)	0.04
chr17:2861947	<i>RAP1GAP2</i>	0.0169 (0.0052)	0.05	0.0143 (0.0047)	0.04	0.0178 (0.0057)	0.09	0.0179 (0.0063)	0.05
chr17:4350829	<i>SPNS3</i>	0.0081 (0.0035)	0.13	0.0087 (0.0031)	0.04	0.005 (0.004)	0.39	0.0086 (0.0042)	0.13
chr17:4917032	<i>KIF1C</i>	0.0115 (0.004)	0.07	0.0106 (0.0035) -0.0127 (0.0063)	0.04	0.0121 (0.0044)	0.10	0.0165 (0.0046)	0.02
chr17:7083015	<i>ASGR1</i>	-0.0163 (0.0071)	0.13	-0.0127 (0.0063)	0.12	-0.0243 (0.0076)	0.09	-0.0257 (0.0082)	0.04

chr17:10541620	<i>MYH3</i>	-0.0022 (0.0007)	0.05	-0.0022 (0.0006)	0.02	-0.0023 (0.0008)	0.09	-0.003 (0.0008)	0.02
chr17:19628421	NA	-0.031 (0.0086)	0.04	-0.0281 (0.0077)	0.02	-0.035 (0.0091)	0.07	-0.0374 (0.0098)	0.02
chr17:27441752	<i>MYO18A</i>	0.0183 (0.0061)	0.06	0.0186 (0.0054)	0.02	0.0152 (0.0068)	0.18	0.0153 (0.0073)	0.13
chr17:39554246	<i>KRT31</i>	-0.0156 (0.0055)	0.07	-0.0163 (0.0047)	0.02	-0.0112 (0.0062)	0.25	-0.015 (0.0066)	0.11
chr17:76850256	<i>TIMP2</i>	-0.0343 (0.0092)	0.04	-0.0324 (0.0079)	0.01	-0.0256 (0.0104)	0.14	-0.0286 (0.0111)	0.08
chr18:9643805	NA	-0.0473 (0.0143)	0.05	-0.043 (0.0126)	0.02	-0.0476 (0.0159)	0.09	-0.0541 (0.0171)	0.04
chr18:47813745	<i>CXXC1</i>	-0.0082 (0.0028)	0.07	-0.0075 (0.0025)	0.04	-0.0068 (0.0032)	0.20	-0.0077 (0.0034)	0.11
chr18:55906325	<i>NEDD4L</i>	-0.0313 (0.0112)	0.07	-0.029 (0.0097)	0.04	-0.0343 (0.0122)	0.10	-0.0396 (0.013)	0.04
chr19:1612208	<i>TCF3</i>	0.0141 (0.0062)	0.13	0.0151 (0.0054)	0.05	0.0131 (0.0068)	0.23	0.0182 (0.0073)	0.08
chr19:2062522	NA	0.0201 (0.0069)	0.07	0.0183 (0.0061)	0.04	0.0238 (0.0076)	0.09	0.0271 (0.0081)	0.04
chr19:2065374	NA	0.0177 (0.0068)	0.09	0.0191 (0.0059)	0.02	0.0178 (0.0074)	0.15	0.0251 (0.0079)	0.04
chr19:2579745	<i>GNG7</i>	-0.0223 (0.0072)	0.05	-0.0203 (0.0064)	0.03	-0.0201 (0.008)	0.13	-0.0218 (0.0087)	0.08
chr19:2706834	NA	-0.0176 (0.0083)	0.14	-0.0187 (0.0073)	0.06	-0.019 (0.0091)	0.20	-0.0285 (0.0095)	0.05
chr19:4278055	<i>SHD</i>	-0.0217 (0.0077)	0.07	-0.022 (0.0066)	0.02	-0.02 (0.0084)	0.15	-0.0257 (0.009)	0.05
chr19:4540065	<i>LRG1</i>	-0.0242 (0.0089)	0.08	-0.021 (0.0079)	0.06	-0.0327 (0.0096)	0.07	-0.0383 (0.0103)	0.02
chr19:17448937	<i>GTPBP3</i>	0.0009 (0.0004)	0.12	0.0009 (0.0003)	0.04	0.0007 (0.0004)	0.28	0.0011 (0.0004)	0.08
chr19:17597999	<i>SLC27A1</i>	0.0105 (0.0049)	0.14	0.0106 (0.0043)	0.07	0.0102 (0.0055)	0.24	0.0165 (0.0057)	0.05
chr19:17631991	<i>PGLS</i>	0.0217 (0.0076)	0.07	0.0243 (0.0065)	0.02	0.0167 (0.0085)	0.22	0.028 (0.0089)	0.04
chr19:19426589	<i>SUGP1</i>	0.0204 (0.0063)	0.05	0.0171 (0.0056)	0.04	0.0188 (0.007)	0.11	0.0167 (0.0076)	0.12
chr19:33889481	<i>PEPD</i>	0.0155 (0.0068)	0.13	0.0195 (0.0058)	0.02	0.0111 (0.0075)	0.33	0.0186 (0.0079)	0.10
chr19:35502231	<i>GRAMD1A</i>	-0.0162 (0.008)	0.16	-0.0192 (0.0069)	0.05	-0.0143 (0.0089)	0.29	-0.0268 (0.0092)	0.05
chr19:40709597	<i>MAP3K10</i>	0.0137 (0.0044)	0.05	0.0117 (0.0039)	0.04	0.0143 (0.0049)	0.10	0.0162 (0.0052)	0.04
chr19:40883570	<i>PLD3</i>	0.0116 (0.0047)	0.11	0.0116 (0.0041)	0.04	0.0111 (0.0052)	0.20	0.016 (0.0055)	0.05
chr19:42557118	<i>GRIK5</i>	0.0147 (0.0055)	0.08	0.0137 (0.0048)	0.04	0.0094 (0.0062)	0.31	0.009 (0.0066)	0.29
chr19:42582914	<i>ZNF574</i>	0.0175 (0.0063)	0.07	0.0173 (0.0055)	0.03	0.018 (0.007)	0.12	0.0228 (0.0073)	0.04
chr20:33543028	<i>GSS</i>	-0.0169 (0.0068)	0.10	-0.015 (0.006)	0.07	-0.0204 (0.0073)	0.10	-0.0223 (0.0078)	0.05
chr20:56419097	NA	0.0092 (0.0045)	0.15	0.0084 (0.004)	0.10	0.0122 (0.0049)	0.14	0.0149 (0.0052)	0.05
chr21:44462317	NA	0.0221 (0.0067)	0.05	0.0192 (0.0059)	0.02	0.0201 (0.0074)	0.11	0.0227 (0.008)	0.05
chr21:44914774	NA	-0.0231 (0.0087)	0.09	-0.0233 (0.0076)	0.04	-0.0272 (0.0096)	0.10	-0.0334 (0.0103)	0.04
chr22:38137445	<i>TRIOBP</i>	-0.0141 (0.0065)	0.13	-0.0154 (0.0056)	0.05	-0.0109 (0.0072)	0.31	-0.0185 (0.0076)	0.09

chr22:39348639	NA	-0.0265 (0.0078)	0.05	-0.0234 (0.0069)	0.02	-0.0288 (0.0086)	0.07	-0.0355 (0.009)	0.02
chrX:48620142	<i>GLOD5</i>	0.0141 (0.0059)	0.12	0.0122 (0.0052)	0.08	0.0164 (0.0065)	0.13	0.0199 (0.0069)	0.05
chrX:68759322	NA	0.0146 (0.0077)	0.17	0.0189 (0.0066)	0.04	-0.0013 (0.0086)	0.92	0.0074 (0.0093)	0.54

<sup>a</sup> Genomic location is according to genome build GRCh37/hg19

<sup>b</sup> Effect estimates represent the change in proportion of DNA methylation at the locus for each ln-transformed unit of the fire-variable in linear mixed effects models adjusted for batch, cell type estimates, Hispanic ethnicity, estimated smoking pack-years, time between baseline and follow-up, and a random intercept for individual. Separate models were run for each fire-variable.

NA means the CpG site is not within a gene or within a known feature (e.g. promoter) of a specific gene.

Statistically significant at q-value<0.05

## SUPPLEMENTAL METHODS

Samples were randomized and hybridized to chips across three batches (one at the University of Utah DNA Sequencing and Genomics Core Facility, and two batches at the University of Michigan Advanced Genomics Core), scanned by experienced personnel, and processed as we previously described.[1] Briefly, raw image files were read with the R package minfi, and the ENmix package was used for quality control and normalization.[2] Probes were removed if at least 5% of samples were not detected ( $p$ -value $>1e^{-16}$  compared to background). Background correction was performed with noob and dye bias correction with Regression on Logarithm of Internal Control probes followed by quantile normalization.[3] Cross-reactive probes and probes with SNPs in the CpG or single-base extension site were excluded. Five pairs that failed quality control for at least one sample were excluded. The final dataset consisted of 759,346 CpG sites and 100 samples (50 pairs).

The proportion of six blood cell types were estimated using reference data from sorted blood leukocytes according to the algorithm established by Houseman *et al.*[4] We used data from control probes included on each chip for surrogate variable analysis, and created three principal components (PCs) explaining 92% of the technical variance in the data; these are used as covariates in downstream models to adjust for batch effects.[5] While all participants were reported to be current non-smokers, past exposure was uncertain. We used an algorithm based on the DNA methylation data to estimate lifetime smoking pack-years.[6] Since this estimation is highly correlated with age, we regressed pack-years on age and adjusted for the residuals in statistical models (referred to as “pack-years residual”).

### References:

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**SUPPLEMENTAL MATERIAL for:**

Repeat Measures of DNA Methylation in an Inception Cohort of Firefighters

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## SUPPLEMENTAL TABLES

**Supplemental Table S1.** All Significantly Differentially Methylated CpG Sites when comparing baseline and follow-up samples from new recruits (q-value<0.05)

Probe ID	Genomic Location <sup>a</sup>	Gene Name	Estimate (SE) <sup>b</sup>	p-value	q-value	CpG site associated with smoking: current vs. never? <sup>c</sup>	CpG site associated with smoking: former vs. never? <sup>c</sup>	Near CpG Island? <sup>d</sup>	Annotation Relative to Nearest Gene <sup>e</sup>
cg13798302	chr4: 100870323	<i>LOC256880</i>	-0.014 (0.002)	1.62E-08	0.01	no	no	North Shore	within 1500 bp of TSS within gene body
cg10874300	chr5: 67588385	<i>PIK3R1</i>	-0.066 (0.011)	4.36E-08	0.01	not tested	not tested	South Shelf	
cg12668515	chr9: 113861165	NA	-0.044 (0.007)	7.36E-08	0.01	not tested	not tested	Open Sea	
cg16668826	chr17: 12448991	NA	0.027 (0.005)	8.93E-08	0.01	not tested	not tested	Open Sea	
cg17636707	chr10: 30970470	NA	0.015 (0.002)	1.09E-07	0.01	no	no	Open Sea	
cg18105361	chr5: 135536668	NA	-0.044 (0.007)	1.06E-07	0.01	no	no	Open Sea	
cg05423480	chr15: 65189594	NA	-0.031 (0.005)	1.65E-07	0.02	not tested	not tested	Open Sea	
cg07280206	chr16: 56554249	<i>BBS2</i>	-0.063 (0.01)	1.61E-07	0.02	no	no	South Shore	within 1500 bp of TSS
cg02923300	chrX: 68759322	NA	0.037 (0.006)	2.87E-07	0.02	no	no	South Shore	
cg04853543	chr17: 77974147	<i>TBC1D16</i>	0.032 (0.006)	2.61E-07	0.02	not tested	not tested	Open Sea	within gene body
cg16216305	chr3: 127842716	<i>RUVBL1</i>	-0.002 (0)	3.06E-07	0.02	no	no	in CpG Island	within 200 bp of TSS
cg27608911	chr3: 115341429	<i>GAP43</i>	0.026 (0.005)	2.48E-07	0.02	no	no	Open Sea	within 1500 bp of TSS within gene body
cg25945533	chr19: 40883570	<i>PLD3</i>	0.023 (0.004)	3.57E-07	0.02	not tested	not tested	North Shelf	within gene body
cg15010903	chr17: 76850256	<i>TIMP2</i>	-0.046 (0.008)	3.90E-07	0.02	no	no	North Shore	3'UTR
cg01152629	chr19: 4705838	<i>DPP9</i>	0.023 (0.004)	4.44E-07	0.02	not tested	not tested	Open Sea	within gene body
cg00156769	chr1: 183498596	<i>SMG7</i>	0.015 (0.003)	1.04E-06	0.02	not tested	not tested	Open Sea	within gene body
cg01092213	chr7: 48127925	<i>UPP1</i>	-0.035 (0.006)	5.99E-07	0.02	no	no	North Shore	within 1500 bp of TSS
cg01739831	chr16: 89922539	<i>SPIRE2</i>	0.029 (0.005)	9.26E-07	0.02	no	no	South Shore	within gene body

cg03740864	chr10: 120660492	NA	-0.054 (0.01)	8.46E-07	0.02	not tested	not tested	Open Sea	
cg03923285	chr16: 412168	NA	-0.046 (0.008)	9.40E-07	0.02	no	no	South Shore	
cg04497992	chr16: 616212	<i>NHLRC4</i>	-0.042 (0.008)	8.60E-07	0.02	no	no	South Shore	within 1500 bp of TSS
cg05463966	chr11: 67803951	<i>NDUFS8</i>	-0.037 (0.007)	1.06E-06	0.02	no	no	North Shelf	within gene body
cg05632631	chr16: 24099614	<i>PRKCB</i>	0.017 (0.003)	1.08E-06	0.02	no	no	Open Sea	within gene body
cg12784120	chr17: 41847254	<i>DUSP3</i>	0.022 (0.004)	5.08E-07	0.02	no	no	Open Sea	within gene body
cg16001875	chr3: 47019411	<i>CCDC12</i>	0.029 (0.005)	6.90E-07	0.02	not tested	not tested	North Shore	within 1500 bp of TSS
cg16353975	chr12: 88531040	<i>CEP290</i>	0.017 (0.003)	1.02E-06	0.02	not tested	not tested	Open Sea	within gene body
cg18676539	chr8: 144575488	<i>ZC3H3</i>	0.025 (0.005)	9.87E-07	0.02	not tested	not tested	Open Sea	within gene body
cg19721787	chr1: 32670695	<i>IQCC</i>	0.035 (0.007)	8.30E-07	0.02	yes	no	in CpG Island	within 1500 bp of TSS
cg19815791	chr17: 76343835	NA	0.027 (0.005)	1.00E-06	0.02	not tested	not tested	Open Sea	
cg21457856	chr3: 148367697	NA	-0.022 (0.004)	1.13E-06	0.02	no	no	Open Sea	
cg22216159	chr3: 109746788	NA	-0.046 (0.009)	1.05E-06	0.02	not tested	not tested	Open Sea	
cg22385591	chr13: 72778607	NA	-0.036 (0.007)	1.14E-06	0.02	not tested	not tested	Open Sea	
cg23477670	chr8: 27114746	<i>STMN4</i>	-0.045 (0.008)	9.73E-07	0.02	not tested	not tested	Open Sea	5'UTR within gene body
cg23532197	chr10: 11908666	<i>C10orf47</i>	-0.033 (0.006)	8.80E-07	0.02	no	no	North Shelf	
cg23865100	chr3: 184344968	NA	-0.044 (0.008)	6.20E-07	0.02	not tested	not tested	Open Sea	
cg24067133	chr11: 79613887	NA	-0.046 (0.009)	7.29E-07	0.02	not tested	not tested	Open Sea	
cg25529557	chr6: 112145775	<i>FYN</i>	-0.044 (0.008)	1.07E-06	0.02	not tested	not tested	Open Sea	5'UTR within gene body
cg25983854	chr22: 47257568	<i>TBC1D22A</i>	0.018 (0.003)	1.03E-06	0.02	no	no	South Shore	within gene body
cg02359589	chr17: 8045663	<i>PER1</i>	0.03 (0.006)	1.19E-06	0.02	no	no	Open Sea	within gene body
cg13783035	chr22: 46154632	<i>ATXN10</i>	0.009 (0.002)	1.22E-06	0.02	not tested	not tested	Open Sea	within gene body
cg12369388	chr2: 47094435	NA	0.02 (0.004)	1.33E-06	0.02	not tested	not tested	Open Sea	
cg15086037	chr2: 40823629	NA	0.012 (0.002)	1.31E-06	0.02	not tested	not tested	Open Sea	
cg00555389	chr2: 178261381	<i>AGPS</i>	-0.04 (0.008)	1.42E-06	0.03	not tested	not tested	South Shelf	within gene body
cg02029108	chr7: 98609251	<i>TRRAP</i>	0.026 (0.005)	1.65E-06	0.03	not tested	not tested	South Shore	within gene body
cg02708501	chr17: 4350829	<i>SPNS3</i>	0.016 (0.003)	1.50E-06	0.03	not tested	not tested	Open Sea	within gene body
cg03779244	chrX: 56771607	<i>LINC01420</i>	-0.085 (0.016)	1.60E-06	0.03	not tested	not tested	Open Sea	within gene body

cg09417137	chr3: 9811912	<i>CAMK1</i>	-0.035 (0.007)	1.65E-06	0.03	not tested	not tested	South Shore	within 1500 bp of TSS
cg13166622	chr3: 150904863	<i>MED12L</i>	-0.081 (0.016)	1.64E-06	0.03	not tested	not tested	Open Sea	within gene body
cg15728672	chr8: 89189971	<i>MMP16</i>	-0.059 (0.011)	1.64E-06	0.03	not tested	not tested	Open Sea	within gene body
cg17214079	chr17: 37719431	NA	0.015 (0.003)	1.62E-06	0.03	not tested	not tested	Open Sea	
cg10992198	chr19: 36552038	<i>WDR62</i>	0.03 (0.006)	1.72E-06	0.03	not tested	not tested	Open Sea	within gene body
cg00137860	chr22: 26249504	<i>MYO18B</i>	-0.04 (0.008)	1.77E-06	0.03	not tested	not tested	Open Sea	within gene body
cg10764756	chr11: 126337070	<i>KIRREL3</i>	0.031 (0.006)	1.82E-06	0.03	not tested	not tested	Open Sea in CpG Island	within gene body
cg16688112	chr16: 88922774	<i>GALNS</i>	-0.029 (0.006)	1.82E-06	0.03	yes	no	Island	within gene body
cg00625110	chr16: 53741731	<i>FTO</i>	0.069 (0.014)	3.35E-06	0.03	no	no	South Shelf	within gene body
cg00949337	chr20: 61181680	NA	0.022 (0.004)	2.65E-06	0.03	not tested	not tested	South Shelf	
cg01622399	chr11: 134387905	NA	-0.04 (0.008)	3.55E-06	0.03	not tested	not tested	Open Sea in CpG Island	
cg01862160	chr9: 135456402	NA	-0.035 (0.007)	3.25E-06	0.03	no	no	Island	
cg02098857	chr17: 27441752	<i>MYO18A</i>	0.028 (0.005)	1.99E-06	0.03	not tested	not tested	Open Sea	within gene body
cg02319637	chrX: 68525486	NA	-0.046 (0.009)	2.43E-06	0.03	not tested	not tested	North Shore	
cg02996608	chr1: 23256885	NA	-0.027 (0.005)	3.05E-06	0.03	not tested	not tested	Open Sea	
cg03776062	chr17: 76390494	<i>PGS1</i>	0.009 (0.002)	3.68E-06	0.03	not tested	not tested	Open Sea	within gene body
cg03897241	chr7: 1808115	NA	0.013 (0.003)	2.03E-06	0.03	no	no	North Shore	
cg04639736	chr4: 142481583	NA	-0.034 (0.007)	2.81E-06	0.03	not tested	not tested	Open Sea	
cg04694057	chr12: 49763589	<i>SPATS2</i>	-0.041 (0.008)	3.35E-06	0.03	not tested	not tested	South Shelf	5'UTR
cg04974344	chr4: 132420800	NA	-0.04 (0.008)	2.64E-06	0.03	not tested	not tested	Open Sea	
cg05419854	chr17: 19398395	NA	0.023 (0.005)	3.38E-06	0.03	no	no	Open Sea	
cg05541640	chr3: 52008740	<i>ABHD14B</i>	-0.036 (0.007)	3.33E-06	0.03	yes	no	North Shore	within 200 bp of TSS
cg05753918	chr7: 14899040	NA	-0.065 (0.013)	2.32E-06	0.03	not tested	not tested	Open Sea	
cg06044060	chr9: 135880142	NA	-0.029 (0.006)	3.30E-06	0.03	not tested	not tested	Open Sea	
cg06492744	chr11: 65406254	<i>SIPA1</i>	-0.005 (0.001)	3.72E-06	0.03	no	no	North Shelf	5'UTR
cg07499197	chr19: 47921090	<i>MEIS3</i>	-0.032 (0.006)	2.80E-06	0.03	not tested	not tested	North Shore	within gene body
cg07664312	chr12: 18433550	<i>PIK3C2G</i>	0.019 (0.004)	3.48E-06	0.03	no	no	Open Sea	5'UTR
cg08448786	chr10: 82258519	<i>TSPAN14</i>	-0.035 (0.007)	3.77E-06	0.03	not tested	not tested	Open Sea	within gene body
cg08766380	chr17: 31107923	<i>MYO1D</i>	-0.039 (0.008)	3.80E-06	0.03	not tested	not tested	Open Sea	within gene body

cg09951898	chr4: 104022073	<i>BDH2</i>	0.015 (0.003)	3.02E-06	0.03	not tested	not tested	Open Sea	within 1500 bp of TSS
cg10353689	chr2: 70792316	NA	0.019 (0.004)	2.34E-06	0.03	not tested	not tested	Open Sea	
cg10778736	chr15: 45406362	<i>DUOX2</i>	-0.029 (0.006)	2.90E-06	0.03	no	no	North Shore	within 200 bp of TSS
cg11764115	chr19: 11660189	<i>CNN1</i>	0.024 (0.005)	2.03E-06	0.03	no	no	North Shore	within gene body
cg11796181	chr5: 142422241	<i>ARHGAP26</i>	0.013 (0.003)	3.11E-06	0.03	no	no	Open Sea	within gene body
cg11985186	chr1: 54964993	NA	-0.031 (0.006)	2.91E-06	0.03	not tested	not tested	North Shore	
cg12248652	chr12: 132703589	<i>GALNT9</i>	-0.056 (0.011)	3.64E-06	0.03	no	no	Open Sea	within gene body
cg12384419	chr2: 202685659	<i>CDK15</i>	-0.021 (0.004)	1.98E-06	0.03	not tested	not tested	Open Sea	within gene body
cg12709085	chr19: 35502231	<i>GRAMD1A</i>	-0.035 (0.007)	2.86E-06	0.03	not tested	not tested	Open Sea	within gene body
cg13092901	chr22: 50965373	<i>TYMP</i>	-0.032 (0.006)	2.89E-06	0.03	yes	yes	Open Sea	in CpG Island
cg14412992	chr5: 125706935	<i>GRAMD3</i>	0.033 (0.007)	3.47E-06	0.03	not tested	not tested	Open Sea	within gene body
cg14705319	chr5: 176938148	<i>DOK3</i>	-0.038 (0.008)	3.26E-06	0.03	no	no	Open Sea	within 1500 bp of TSS
cg15155209	chr3: 14502277	<i>SLC6A6</i>	0.022 (0.004)	3.14E-06	0.03	no	no	Open Sea	within gene body
cg15168816	chr6: 17282533	<i>RBM24</i>	-0.031 (0.006)	3.83E-06	0.03	no	no	South Shore	within 1500 bp of TSS
cg15281614	chr1: 160345932	NA	-0.042 (0.008)	2.76E-06	0.03	not tested	not tested	Open Sea	
cg15734764	chr10: 134266555	NA	-0.029 (0.006)	2.25E-06	0.03	no	no	North Shore	
cg16262572	chr2: 122479703	<i>NIFK-AS1</i>	-0.052 (0.01)	2.53E-06	0.03	not tested	not tested	Open Sea	within gene body
cg17353568	chr10: 76661092	<i>KAT6B</i>	-0.043 (0.009)	3.33E-06	0.03	not tested	not tested	Open Sea	within gene body
cg17410093	chr2: 232650620	<i>COPS7B</i>	0.023 (0.005)	1.90E-06	0.03	not tested	not tested	North Shore	within 1500 bp of TSS
cg17777792	chr1: 226285808	NA	-0.036 (0.007)	3.05E-06	0.03	not tested	not tested	Open Sea	
cg18032827	chr1: 185227307	<i>SWT1</i>	0.027 (0.005)	3.34E-06	0.03	not tested	not tested	Open Sea	within gene body
cg18164926	chr11: 62600230	<i>STX5</i>	-0.041 (0.008)	2.23E-06	0.03	not tested	not tested	South Shore	within 1500 bp of TSS
cg18661379	chr10: 104393081	<i>SUFU</i>	-0.029 (0.006)	2.89E-06	0.03	no	no	Open Sea	3'UTR
cg18956104	chr12: 119621039	<i>HSPB8</i>	-0.059 (0.012)	3.68E-06	0.03	not tested	not tested	Open Sea	within gene body
cg19465330	chr11: 61084101	<i>DDB1</i>	0.023 (0.005)	3.81E-06	0.03	not tested	not tested	Open Sea	within gene body

cg19842279	chr17: 39554246	<i>KRT31</i>	-0.024 (0.005)	3.69E-06	0.03	not tested	not tested	Open Sea	within 1500 bp of TSS
cg19882915	chr8: 102451058	NA	0.024 (0.005)	3.44E-06	0.03	no	no	Open Sea	
cg21146224	chr9: 13492139	NA	-0.032 (0.006)	3.06E-06	0.03	not tested	not tested	Open Sea	
cg21289437	chr13: 112692270	NA	0.025 (0.005)	3.55E-06	0.03	no	no	South Shore	
cg21611056	chr20: 3776172	<i>CDC25B</i>	-0.038 (0.007)	2.73E-06	0.03	not tested	not tested	North Shore	within 1500 bp of TSS
cg21723874	chr19: 51531123	<i>KLK11</i>	0.036 (0.007)	2.84E-06	0.03	not tested	not tested	Open Sea	5'UTR
cg22071573	chr19: 8506975	NA	0.026 (0.005)	2.99E-06	0.03	not tested	not tested	North Shelf	
cg24144259	chr5: 88875631	NA	-0.042 (0.008)	3.65E-06	0.03	not tested	not tested	Open Sea	
cg24924295	chr17: 999104	<i>ABR</i>	-0.029 (0.006)	3.54E-06	0.03	not tested	not tested	Open Sea	within gene body
cg26128821	chr19: 19511134	<i>GATAD2A</i>	0.026 (0.005)	2.83E-06	0.03	not tested	not tested	Open Sea	5'UTR
cg26859666	chr1: 167883298	<i>ADCY10</i>	0.011 (0.002)	3.29E-06	0.03	no	no	Open Sea in CpG Island	within 1st exon
cg27380788	chr16: 4526765	<i>HMOX2</i>	0.003 (0.001)	3.85E-06	0.03	no	no	Open Sea	5'UTR
cg27639525	chr1: 25029378	NA	0.021 (0.004)	2.89E-06	0.03	not tested	not tested	Open Sea in CpG Island	
cg00187535	chr19: 7747028	<i>TRAPPC5</i>	-0.038 (0.008)	3.92E-06	0.03	no	no	Open Sea	5'UTR
cg25502462	chrX: 48620142	<i>GLOD5</i>	0.027 (0.005)	4.03E-06	0.03	no	no	Open Sea	within 200 bp of TSS
cg07241925	chr4: 1294566	<i>MAEA</i>	-0.029 (0.006)	4.07E-06	0.03	no	no	Open Sea	within gene body
cg03914662	chr11: 65910130	<i>PACS1</i>	-0.035 (0.007)	4.23E-06	0.03	not tested	not tested	Open Sea	within gene body
cg07589116	chr11: 123450089	<i>GRAMD1B</i>	0.024 (0.005)	4.21E-06	0.03	not tested	not tested	South Shore	within gene body
cg13087441	chr1: 3277000	<i>PRDM16</i>	0.027 (0.006)	4.22E-06	0.03	no	no	South Shore	within gene body
cg24851859	chr5: 27532684	NA	-0.047 (0.009)	4.14E-06	0.03	yes	no	Open Sea	
cg06230410	chr19: 19457887	<i>MAU2</i>	0.016 (0.003)	4.33E-06	0.03	not tested	not tested	Open Sea	within gene body
cg12354960	chr1: 156816460	<i>NTRK1</i>	0.02 (0.004)	4.34E-06	0.03	not tested	not tested	South Shore	within gene body
cg18062128	chr2: 97501603	NA	0.02 (0.004)	4.35E-06	0.03	no	no	North Shelf	
cg10015051	chr16: 65102943	<i>CDH11</i>	0.019 (0.004)	4.50E-06	0.03	no	no	Open Sea	5'UTR
cg11360415	chr17: 1059336	<i>ABR</i>	0.022 (0.005)	4.61E-06	0.03	not tested	not tested	Open Sea	within gene body
cg11835575	chr1: 3447205	<i>MEGF6</i>	-0.03 (0.006)	4.59E-06	0.03	not tested	not tested	North Shore	within gene body
cg12018852	chr7: 138777233	<i>ZC3HAV1</i>	-0.052 (0.01)	4.63E-06	0.03	not tested	not tested	Open Sea	within gene body

cg16327381	chr3: 119498036	<i>NR1I2</i>	0.031 (0.006)	4.63E-06	0.03	no	no	Open Sea	within 1500 bp of TSS
cg23222095	chr12: 27934956	<i>KLHL42</i>	0.012 (0.003)	4.51E-06	0.03	not tested	not tested	South Shore	within gene body
cg24418298	chr7: 2752273	<i>AMZ1</i>	0.024 (0.005)	4.61E-06	0.03	no	no	Open Sea	within gene body
cg27423238	chr16: 1420171	<i>UNKL</i>	0.024 (0.005)	4.51E-06	0.03	no	no	in CpG Island	within gene body
cg03762984	chr11: 29355671	NA	-0.081 (0.016)	4.70E-06	0.03	not tested	not tested	Open Sea	
cg03922340	chr3: 49397232	<i>GPX1</i>	-0.035 (0.007)	4.70E-06	0.03	not tested	not tested	South Shore	within 1500 bp of TSS
cg02121135	chr14: 24858912	NA	-0.073 (0.015)	4.82E-06	0.03	not tested	not tested	Open Sea	
cg02984966	chr18: 21266734	NA	-0.032 (0.007)	4.89E-06	0.03	no	no	North Shelf	
cg13212159	chr17: 38075554	<i>GSDMB</i>	0.022 (0.004)	4.90E-06	0.03	no	no	Open Sea	within 1500 bp of TSS
cg06692153	chr22: 38137445	<i>TRIOBP</i>	-0.028 (0.006)	4.95E-06	0.03	not tested	not tested	Open Sea	within gene body
cg11339587	chr19: 30298341	NA	0.024 (0.005)	5.02E-06	0.03	no	no	North Shelf	
cg15468600	chr7: 101633200	<i>CUX1</i>	0.026 (0.005)	5.04E-06	0.03	not tested	not tested	Open Sea	within gene body
cg03197505	chr19: 17597999	<i>SLC27A1</i>	0.022 (0.004)	5.08E-06	0.03	no	no	in CpG Island	within gene body
cg09044656	chr12: 130184851	<i>TMEM132D</i>	0.03 (0.006)	5.26E-06	0.03	no	no	in CpG Island	within gene body
cg16416987	chr1: 155177561	<i>THBS3</i>	-0.033 (0.007)	5.18E-06	0.03	no	no	North Shore	within gene body
cg21368996	chr2: 201593511	<i>AOX2P</i>	-0.029 (0.006)	5.26E-06	0.03	not tested	not tested	Open Sea	within gene body
cg25296103	chr2: 145268533	<i>ZEB2</i>	-0.06 (0.012)	5.25E-06	0.03	no	no	Open Sea	within gene body
cg16802508	chr11: 67070738	<i>SSH3</i>	-0.032 (0.006)	5.36E-06	0.03	no	no	North Shore	within 200 bp of TSS
cg03541759	chr5: 72794079	<i>BTF3</i>	-0.004 (0.001)	5.41E-06	0.03	no	no	in CpG Island	within 200 bp of TSS
cg07488549	chr10: 106052976	<i>GSTO2</i>	-0.042 (0.008)	5.52E-06	0.03	not tested	not tested	Open Sea	within gene body
cg17654217	chr7: 100282651	<i>GIGYF1</i>	0.021 (0.004)	5.50E-06	0.03	no	no	North Shelf	within gene body
cg16238149	chr13: 111173329	NA	-0.031 (0.006)	5.62E-06	0.03	no	no	Open Sea	
cg03933550	chr18: 55906325	<i>NEDD4L</i>	-0.048 (0.01)	5.78E-06	0.03	not tested	not tested	Open Sea	within gene body
cg07872794	chr5: 117897957	<i>HRAT56</i>	0.015 (0.003)	5.90E-06	0.03	not tested	not tested	Open Sea	within 200 bp of TSS
cg11887996	chr12: 120559003	NA	-0.027 (0.006)	5.85E-06	0.03	no	no	South Shelf	

cg13170967	chr5: 38695390	<i>OSMR-AS1</i>	-0.036 (0.007)	5.84E-06	0.03	not tested	not tested	Open Sea	within gene body
cg13304430	chr9: 139414185	<i>MIR4673</i>	0.01 (0.002)	5.88E-06	0.03	not tested	not tested	South Shore	within 200 bp of TSS
cg18742528	chr6: 13053520	<i>PHACTR1</i>	-0.055 (0.011)	5.83E-06	0.03	not tested	not tested	Open Sea	within gene body
cg00841090	chr17: 2651101	NA	-0.027 (0.006)	5.98E-06	0.03	no	no	North Shore	
cg06551987	chr21: 28563103	NA	0.018 (0.004)	6.01E-06	0.03	not tested	not tested	Open Sea in CpG Island	
cg02956806	chr9: 140174741	<i>C9orf167</i>	0.031 (0.006)	6.13E-06	0.03	no	no		3'UTR within gene body
cg03083251	chr7: 135408513	<i>SLC13A4</i>	-0.076 (0.016)	6.70E-06	0.03	not tested	not tested	Open Sea	
cg03432196	chr18: 9643805	NA	-0.063 (0.013)	6.43E-06	0.03	not tested	not tested	Open Sea	
cg04483304	chr15: 68933603	<i>CORO2B</i>	0.021 (0.004)	6.61E-06	0.03	not tested	not tested	Open Sea	5'UTR within gene body
cg04571417	chr16: 11224056	<i>CLEC16A</i>	0.021 (0.004)	6.73E-06	0.03	not tested	not tested	Open Sea	
cg06016751	chr12: 6442329	<i>TNFRSF1A</i>	-0.034 (0.007)	6.53E-06	0.03	not tested	not tested	South Shelf	ExonBnd within gene body
cg06285037	chr7: 131233012	<i>PODXL</i>	0.021 (0.004)	6.53E-06	0.03	not tested	not tested	Open Sea in CpG Island	
cg10884953	chr19: 2579745	<i>GNG7</i>	-0.031 (0.006)	6.65E-06	0.03	no	no	Island	5'UTR
cg11362074	chr19: 2706834	NA	-0.035 (0.007)	6.82E-06	0.03	no	no	South Shelf	
cg14611112	chr9: 139643351	<i>LCN6</i>	-0.053 (0.011)	6.49E-06	0.03	no	no	South Shelf	within 1500 bp of TSS
cg14678981	chr16: 57662244	<i>ADGRG1</i>	-0.026 (0.005)	6.81E-06	0.03	not tested	not tested	Open Sea	within 1st exon
cg15105253	chr14: 100063248	<i>CCDC85C</i>	0.014 (0.003)	6.66E-06	0.03	not tested	not tested	Open Sea in CpG Island	within gene body
cg15198739	chr22: 26908541	<i>TFIP11</i>	-0.003 (0.001)	6.32E-06	0.03	no	no	Island	within 200 bp of TSS
cg15300024	chr2: 113487167	NA	-0.029 (0.006)	6.53E-06	0.03	not tested	not tested	Open Sea	
cg20253556	chr10: 30712431	NA	-0.028 (0.006)	6.43E-06	0.03	not tested	not tested	Open Sea	
cg21346966	chr2: 238341793	NA	-0.022 (0.005)	6.15E-06	0.03	no	no	Open Sea	
cg24105728	chr6: 13007033	<i>PHACTR1</i>	-0.054 (0.011)	6.61E-06	0.03	not tested	not tested	Open Sea	within gene body
cg24668049	chr16: 88614791	NA	-0.036 (0.007)	6.32E-06	0.03	not tested	not tested	Open Sea	
cg25229577	chr3: 58367583	<i>PXK</i>	0.062 (0.013)	6.81E-06	0.03	not tested	not tested	Open Sea	5'UTR within 200 bp of TSS
cg26833538	chr11: 67777715	<i>ALDH3B1</i>	-0.03 (0.006)	6.29E-06	0.03	yes	no	Open Sea	
cg05166976	chr2: 242842459	NA	0.022 (0.005)	6.95E-06	0.03	no	no	North Shore	
cg16054275	chr1: 169556022	<i>F5</i>	-0.038 (0.008)	6.91E-06	0.03	no	no	Open Sea	within 1500 bp of TSS
cg19677181	chr5: 153211415	NA	-0.042 (0.009)	6.91E-06	0.03	not tested	not tested	Open Sea	
cg16594092	chr5: 169911303	<i>KCNIP1</i>	-0.028 (0.006)	7.09E-06	0.03	not tested	not tested	Open Sea	within gene body



cg21455534	chr6: 170101504 chr13: 110124427	<i>C6orf120</i>	0.009 (0.002)	7.11E-06	0.03	no	no	North Shore	within 1500 bp of TSS
cg01387115		NA	-0.024 (0.005)	7.23E-06	0.03	not tested	not tested	Open Sea	
cg13418283	chr20: 61439240 chr12: 131273144	<i>OGFR</i>	0.025 (0.005)	7.32E-06	0.03	not tested	not tested	North Shelf	within gene body
cg05410283		NA	0.014 (0.003)	7.52E-06	0.03	no	no	Open Sea	
cg16903817	chr2: 114655480	<i>ACTR3</i>	-0.09 (0.019)	7.62E-06	0.03	not tested	not tested	Open Sea	5'UTR
cg10967759	chr10: 73555025	<i>CDH23</i>	-0.071 (0.015)	7.81E-06	0.03	not tested	not tested	Open Sea	within 1500 bp of TSS
cg23926670	chr12: 28121938	<i>PTHLH</i>	0.044 (0.009)	7.77E-06	0.03	no	no	North Shore	within gene body
cg10175261	chr20: 56419097	NA	0.02 (0.004)	7.90E-06	0.03	not tested	not tested	Open Sea	
cg02928345	chr1: 224411698	NA	-0.065 (0.014)	8.08E-06	0.03	no	no	Open Sea	
cg06753606	chr17: 40337708	<i>HCRT</i>	0.021 (0.004)	8.02E-06	0.03	not tested	not tested	South Shore	within 1500 bp of TSS
cg18066598	chr8: 64992450	NA	-0.046 (0.009)	8.05E-06	0.03	no	no	Open Sea	
cg16265542	chr1: 152814831 chr10: 108337483	<i>LCE6A</i>	-0.058 (0.012)	8.23E-06	0.03	no	no	Open Sea	within 1500 bp of TSS
cg26914953		<i>SORCS1</i>	-0.031 (0.006)	8.21E-06	0.03	not tested	not tested	Open Sea	within gene body
cg00599564	chr6: 29943209	<i>HCG9</i>	-0.025 (0.005)	8.35E-06	0.03	no	no	North Shore	within gene body
cg07551022	chr1: 205760086	<i>SLC41A1</i>	0.01 (0.002)	8.52E-06	0.03	no	no	Open Sea	3'UTR
cg18667648	chr11: 6626577	<i>ILK</i>	-0.034 (0.007)	8.35E-06	0.03	not tested	not tested	South Shore	5'UTR
cg21857190	chr2: 217913299	NA	-0.019 (0.004)	8.53E-06	0.03	no	no	Open Sea	
cg22867941	chr4: 1225044	<i>CTBP1</i>	0.032 (0.007)	8.50E-06	0.03	not tested	not tested	South Shore in CpG Island	within gene body
cg23098305	chr1: 228112951	<i>WNT9A</i>	0.034 (0.007)	8.37E-06	0.03	no	no		within gene body
cg25303556	chr22: 39348639	NA	-0.034 (0.007)	8.46E-06	0.03	not tested	not tested	Open Sea	
cg03515346	chr4: 1645766	<i>FAM53A</i>	0.016 (0.003)	8.82E-06	0.03	not tested	not tested	North Shore	within gene body
cg08295857	chr16: 88096588	<i>BANP</i>	0.032 (0.007)	9.00E-06	0.03	no	no	Open Sea	within gene body
cg13387425	chr12: 54402050	<i>HOXC8</i>	-0.032 (0.007)	8.99E-06	0.03	not tested	not tested	North Shore	within 1500 bp of TSS
cg14099540	chr9: 136018794	<i>RALGDS</i>	-0.032 (0.007)	9.00E-06	0.03	no	no	North Shore	within gene body
cg22306344	chr3: 49966773	<i>MON1A</i>	0.01 (0.002)	9.02E-06	0.03	no	no	North Shore	within gene body
cg11138095	chr13: 49794053	<i>MLNR</i>	-0.033 (0.007)	9.08E-06	0.03	no	no	North Shore	within 1500 bp of TSS

cg25181302	chr17: 74570181	<i>ST6GALNAC2</i>	0.02 (0.004)	9.19E-06	0.03	not tested	not tested	Open Sea	within gene body
cg00325383	chr6: 85404488	<i>LOC102724201</i>	-0.057 (0.012)	9.43E-06	0.03	not tested	not tested	Open Sea	within gene body
cg11073382	chr4: 120898808	NA	-0.04 (0.008)	9.47E-06	0.03	no	no	Open Sea	
cg11644454	chr1: 172417035	<i>C1orf105</i>	-0.036 (0.007)	9.45E-06	0.03	not tested	not tested	South Shelf	within gene body
cg18411043	chr1: 31221135	<i>LAPTM5</i>	-0.024 (0.005)	9.36E-06	0.03	no	no	Open Sea	within gene body
cg20118823	chr19: 1612208	<i>TCF3</i>	0.025 (0.005)	9.33E-06	0.03	no	no	North Shelf	within gene body
cg02383650	chr11: 3050362	<i>CARS</i>	0.019 (0.004)	9.61E-06	0.03	not tested	not tested	Open Sea	within gene body
cg02428178	chr15: 49104237	<i>CEP152</i>	-0.053 (0.011)	9.69E-06	0.03	no	no	South Shore	within 1500 bp of TSS
cg04255090	chr16: 85343936	NA	-0.03 (0.006)	9.72E-06	0.03	not tested	not tested	Open Sea	
cg11175192	chr2: 219724918	<i>WNT6</i>	-0.034 (0.007)	9.57E-06	0.03	no	no	in CpG Island	within gene body
cg17357892	chr21: 44914774	NA	-0.036 (0.008)	9.72E-06	0.03	not tested	not tested	Open Sea	
cg24935208	chr3: 89097455	NA	-0.031 (0.007)	9.77E-06	0.03	no	no	Open Sea	
cg10702418	chr7: 157090031	NA	-0.049 (0.01)	9.91E-06	0.03	no	no	North Shelf	
cg12587260	chr14: 73703163	<i>PAPLN</i>	-0.038 (0.008)	9.87E-06	0.03	not tested	not tested	North Shore	within 1500 bp of TSS
cg13979872	chr19: 44327981	NA	0.017 (0.004)	9.85E-06	0.03	no	no	South Shelf	
cg12202498	chr3: 15482605	<i>EAF1</i>	-0.026 (0.005)	9.97E-06	0.03	not tested	not tested	Open Sea	3'UTR
cg21907521	chr19: 49255510	<i>FUT1</i>	-0.029 (0.006)	1.01E-05	0.03	not tested	not tested	South Shore	5'UTR
cg25579675	chr14: 23846906	<i>CMTM5</i>	-0.03 (0.006)	1.03E-05	0.03	no	no	Open Sea	within gene body
cg07100050	chr10: 21390114	<i>NEBL</i>	-0.047 (0.01)	1.04E-05	0.03	not tested	not tested	Open Sea	within gene body
cg08141463	chr3: 119310381	NA	0.013 (0.003)	1.07E-05	0.03	no	no	Open Sea	
cg11369971	chr12: 15337635	<i>RERG</i>	-0.035 (0.007)	1.07E-05	0.03	not tested	not tested	Open Sea	within gene body
cg13766864	chr11: 74172851	<i>KCNE3</i>	-0.048 (0.01)	1.05E-05	0.03	no	no	Open Sea	5'UTR
cg16551513	chr8: 134261857	<i>NDRG1</i>	-0.043 (0.009)	1.07E-05	0.03	not tested	not tested	Open Sea	within gene body
cg22599985	chr12: 51420538	<i>SLC11A2</i>	-0.027 (0.006)	1.06E-05	0.03	not tested	not tested	South Shore	within 1500 bp of TSS
cg23199873	chr7: 93090748	<i>CALCR</i>	-0.045 (0.009)	1.06E-05	0.03	not tested	not tested	Open Sea	within gene body
cg24214000	chr22: 50282386	<i>ZBED4</i>	0.021 (0.004)	1.04E-05	0.03	no	no	South Shelf	3'UTR
cg24954207	chr3: 128217091	NA	-0.039 (0.008)	1.07E-05	0.03	no	no	South Shore	
cg11835347	chr1: 113248232	<i>RHOC</i>	-0.054 (0.011)	1.09E-05	0.04	yes	no	North Shore	5'UTR
cg14457284	chr9: 135852984	<i>GFI1B</i>	-0.04 (0.008)	1.09E-05	0.04	no	no	Open Sea	within 1500 bp of TSS

cg03498271	chr5: 38427885	<i>EGFLAM</i>	-0.055 (0.012)	1.12E-05	0.04	not tested	not tested	Open Sea	within gene body
cg15228983	chr19: 42582914	<i>ZNF574</i>	0.026 (0.005)	1.12E-05	0.04	no	no	North Shore	within gene body
cg07164136	chr10: 108393920	<i>SORCS1</i>	-0.025 (0.005)	1.13E-05	0.04	no	no	Open Sea in CpG Island	within gene body
cg10043090	chr11: 1536810	<i>HCCA2</i>	-0.047 (0.01)	1.14E-05	0.04	no	no	Island	within gene body
cg09554514	chr4: 186693893	<i>SORBS2</i>	-0.036 (0.008)	1.16E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg11482105	chr1: 56241150	NA	-0.033 (0.007)	1.17E-05	0.04	not tested	not tested	Open Sea	
cg13019856	chr2: 70945292	<i>ADD2</i>	-0.042 (0.009)	1.17E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg20907456	chr11: 57405372	NA	-0.029 (0.006)	1.17E-05	0.04	yes	no	Open Sea	
cg13846358	chr9: 135115582	<i>NTNG2</i>	0.032 (0.007)	1.18E-05	0.04	no	no	North Shore	within gene body
cg00216061	chr16: 88547579	<i>ZFPM1</i>	0.025 (0.005)	1.19E-05	0.04	no	no	Open Sea	within gene body
cg14174894	chr19: 42557118	<i>GRIK5</i>	0.023 (0.005)	1.19E-05	0.04	not tested	not tested	Open Sea	within gene body
cg03388769	chr5: 60622671	NA	0.032 (0.007)	1.22E-05	0.04	not tested	not tested	North Shelf	
cg13697368	chr17: 7833663	<i>TRAPPC1</i>	0.02 (0.004)	1.21E-05	0.04	no	no	North Shore	3'UTR
cg26877588	chr18: 61455379	<i>SERPINB7</i>	0.019 (0.004)	1.21E-05	0.04	no	no	Open Sea	within gene body
cg08188318	chr6: 34984953	<i>ANKS1A</i>	-0.093 (0.02)	1.24E-05	0.04	no	no	Open Sea	within gene body
cg12474404	chr14: 102814892	<i>CINP</i>	0.022 (0.005)	1.24E-05	0.04	not tested	not tested	Open Sea	3'UTR
cg12840850	chr20: 62407352	<i>ZBTB46</i>	0.021 (0.005)	1.24E-05	0.04	no	no	South Shore in CpG Island	within gene body
cg27250841	chr18: 47813745	<i>CXXC1</i>	-0.012 (0.003)	1.24E-05	0.04	no	no	Island	within gene body
cg00535807	chr9: 5186210	<i>INSL6</i>	0.015 (0.003)	1.31E-05	0.04	not tested	not tested	South Shore	within 1500 bp of TSS
cg00718684	chr6: 31692026	<i>C6orf25</i>	0.041 (0.009)	1.33E-05	0.04	no	no	South Shore	within gene body
cg01078446	chr12: 115113212	<i>TBX3</i>	-0.05 (0.01)	1.31E-05	0.04	no	no	South Shore	within gene body
cg01327863	chr11: 64878267	<i>TM7SF2</i>	-0.028 (0.006)	1.30E-05	0.04	not tested	not tested	North Shore	within 1500 bp of TSS
cg01461514	chr7: 55177182	<i>EGFR</i>	-0.044 (0.009)	1.26E-05	0.04	no	no	Open Sea	within gene body
cg04009045	chr2: 74804817	<i>M1AP</i>	-0.027 (0.006)	1.27E-05	0.04	not tested	not tested	Open Sea	within gene body
cg04179940	chr20: 33871836	<i>EIF6</i>	-0.032 (0.007)	1.34E-05	0.04	yes	no	North Shore	within gene body
cg06042828	chr16: 68058281	<i>DDX28</i>	-0.022 (0.005)	1.34E-05	0.04	no	no	South Shore	within 1500 bp of TSS

cg07520586	chr17: 2861947	<i>RAP1GAP2</i>	0.022 (0.005)	1.32E-05	0.04	not tested	not tested	Open Sea	within gene body
cg08356805	chr16: 88979098	<i>CBFA2T3</i>	0.023 (0.005)	1.29E-05	0.04	no	no	South Shelf	5'UTR
cg08509749	chr13: 65884209	NA	0.028 (0.006)	1.34E-05	0.04	no	no	Open Sea	
cg09396490	chr9: 126372395	<i>DENND1A</i>	0.02 (0.004)	1.34E-05	0.04	not tested	not tested	Open Sea	within gene body
cg10271993	chr8: 110593242	<i>SYBU</i>	-0.034 (0.007)	1.32E-05	0.04	not tested	not tested	Open Sea	within gene body
cg14561649	chr2: 240044446	<i>HDAC4</i>	0.025 (0.005)	1.31E-05	0.04	not tested	not tested	North Shore	within gene body
cg15547507	chr2: 232557565	NA	0.023 (0.005)	1.28E-05	0.04	not tested	not tested	Open Sea	
cg16049584	chr10: 93735638	<i>BTAF1</i>	0.011 (0.002)	1.31E-05	0.04	not tested	not tested	Open Sea	within gene body
cg18670934	chr8: 128512692	NA	0.013 (0.003)	1.32E-05	0.04	not tested	not tested	Open Sea	
cg19890584	chr13: 100024488	<i>UBAC2</i>	-0.04 (0.008)	1.31E-05	0.04	not tested	not tested	Open Sea	within gene body
cg20538322	chr12: 114851913	NA	0.028 (0.006)	1.29E-05	0.04	no	no	North Shore	
cg06297541	chr16: 22384949	<i>CDR2</i>	-0.053 (0.011)	1.35E-05	0.04	no	no	North Shore	within gene body
cg01593812	chr21: 35312645	<i>LINC00649</i>	-0.033 (0.007)	1.36E-05	0.04	not tested	not tested	Open Sea	within gene body
cg04270823	chr20: 62687554	<i>TCEA2</i>	-0.044 (0.009)	1.36E-05	0.04	not tested	not tested	North Shore	within 1500 bp of TSS
cg10835711	chr8: 77618141	<i>ZFHX4</i>	0.031 (0.007)	1.37E-05	0.04	no	no	Open Sea	within gene body
cg12983664	chr13: 110441015	NA	-0.047 (0.01)	1.38E-05	0.04	not tested	not tested	South Shore	
cg14018648	chr17: 7083015	<i>ASGR1</i>	-0.03 (0.006)	1.40E-05	0.04	no	no	Open Sea	within 200 bp of TSS
cg19933810	chr16: 1386290	<i>BAIAP3</i>	-0.031 (0.007)	1.41E-05	0.04	not tested	not tested	South Shore	5'UTR
cg23383111	chr15: 51742890	<i>DMXL2</i>	0.018 (0.004)	1.41E-05	0.04	not tested	not tested	Open Sea	within gene body
cg24418941	chr19: 2062522	NA	0.028 (0.006)	1.40E-05	0.04	yes	no	South Shore	
cg21019063	chr15: 98065112	<i>LOC101927286</i>	-0.048 (0.01)	1.42E-05	0.04	not tested	not tested	Open Sea	within 200 bp of TSS
cg08548535	chr4: 155661052	NA	0.014 (0.003)	1.43E-05	0.04	no	no	North Shore	
cg08813149	chr1: 192736213	NA	-0.016 (0.004)	1.43E-05	0.04	not tested	not tested	Open Sea	
cg13805711	chr4: 6374101	<i>PPP2R2C</i>	0.024 (0.005)	1.44E-05	0.04	not tested	not tested	Open Sea	within gene body
cg04339947	chr11: 61443052	NA	0.028 (0.006)	1.46E-05	0.04	no	no	Open Sea	
cg06980173	chr1: 154376344	<i>IL6R</i>	-0.047 (0.01)	1.47E-05	0.04	yes	no	North Shore	within 1500 bp of TSS
cg07169009	chr20: 1607919	NA	0.026 (0.006)	1.47E-05	0.04	not tested	not tested	Open Sea	
cg14187236	chr17: 49205442	NA	0.022 (0.005)	1.47E-05	0.04	not tested	not tested	Open Sea	

cg10075503	chr19: 752097	<i>MISP</i>	0.018 (0.004)	1.49E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg10635343	chr5: 39378426	<i>DAB2</i>	0.009 (0.002)	1.49E-05	0.04	not tested	not tested	Open Sea	within gene body
cg12122387	chr8: 17756185	NA	-0.041 (0.008)	1.49E-05	0.04	not tested	not tested	Open Sea	
cg00764771	chr7: 150086034	<i>ZNF775</i>	-0.047 (0.01)	1.55E-05	0.04	not tested	not tested	Open Sea	within gene body
cg03627489	chr16: 51341199	NA	-0.033 (0.007)	1.54E-05	0.04	no	no	Open Sea	
cg04474832	chr3: 52008487	<i>ABHD14B</i>	-0.032 (0.007)	1.51E-05	0.04	no	no	North Shore	within 1st exon
cg04959662	chr2: 109941286	<i>SH3RF3</i>	0.009 (0.002)	1.57E-05	0.04	not tested	not tested	Open Sea	within gene body
cg08879394	chr7: 111162222	<i>IMMP2L</i>	0.013 (0.003)	1.53E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg08971940	chr10: 36214839	NA	0.016 (0.003)	1.54E-05	0.04	no	no	Open Sea	
cg09295164	chr11: 85904644	NA	-0.006 (0.001)	1.58E-05	0.04	not tested	not tested	Open Sea	
cg11474135	chr4: 113933301	<i>ANK2</i>	-0.047 (0.01)	1.51E-05	0.04	no	no	Open Sea	within gene body
cg14155327	chr4: 87235054	<i>MAPK10</i>	-0.04 (0.009)	1.57E-05	0.04	no	no	Open Sea	5'UTR
cg14323608	chr19: 13873961	<i>MRI1</i>	0.028 (0.006)	1.57E-05	0.04	no	no	North Shore	within 1500 bp of TSS
cg17433369	chr9: 129938408	<i>RALGPS1</i>	-0.014 (0.003)	1.57E-05	0.04	not tested	not tested	Open Sea	within gene body
cg21156439	chr9: 94716496	NA	0.051 (0.011)	1.57E-05	0.04	no	no	South Shelf	
cg23222717	chr6: 46462509	NA	0.027 (0.006)	1.52E-05	0.04	no	no	South Shelf	
cg26918607	chr2: 216312473	NA	-0.039 (0.008)	1.56E-05	0.04	not tested	not tested	Open Sea	
cg27260887	chr12: 52435577	<i>NR4A1</i>	-0.029 (0.006)	1.51E-05	0.04	not tested	not tested	South Shelf	within gene body
cg07775790	chr5: 169145735	<i>DOCK2</i>	0.009 (0.002)	1.58E-05	0.04	not tested	not tested	Open Sea	within gene body
cg27418500	chr2: 123758682	NA	0.021 (0.005)	1.59E-05	0.04	no	no	Open Sea	
cg01089519	chr11: 46686440	<i>ATG13</i>	0.02 (0.004)	1.62E-05	0.04	not tested	not tested	Open Sea	within gene body
cg01154210	chr21: 27493310	<i>APP</i>	0.102 (0.022)	1.63E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg02719154	chr4: 111533823	NA	-0.033 (0.007)	1.62E-05	0.04	no	no	South Shore	
cg10504000	chr11: 2402391	<i>CD81</i>	-0.04 (0.009)	1.63E-05	0.04	no	no	South Shelf	within gene body
cg11937241	chr4: 135122152	<i>PABPC4L</i>	0.028 (0.006)	1.63E-05	0.04	no	no	Open Sea	within gene body
cg20500791	chr7: 50420285	<i>IKZF1</i>	-0.042 (0.009)	1.61E-05	0.04	not tested	not tested	Open Sea	within gene body
cg12380764	chr1: 206971195	<i>IL19</i>	-0.039 (0.008)	1.65E-05	0.04	no	no	Open Sea	within 1500 bp of TSS
cg02098967	chr2: 241990667	<i>SNED1</i>	0.023 (0.005)	1.66E-05	0.04	not tested	not tested	North Shore	within gene body
cg04946588	chr7: 86271783	<i>GRM3</i>	-0.052 (0.011)	1.66E-05	0.04	not tested	not tested	Open Sea	within 1500 bp of TSS

cg00082998	chr19: 4008627	<i>PIAS4</i>	-0.027 (0.006)	1.69E-05	0.04	not tested	not tested	South Shore	within gene body
cg01761595	chr8: 9821723	NA	-0.069 (0.015)	1.70E-05	0.04	no	no	Open Sea	
cg02884943	chr10: 72725905	NA	-0.059 (0.013)	1.71E-05	0.04	not tested	not tested	Open Sea	
cg04953061	chr14: 53620393	<i>DDHD1</i>	-0.028 (0.006)	1.73E-05	0.04	no	no	South Shore	within 1500 bp of TSS
cg05703302	chr1: 16279468	<i>ZBTB17</i>	-0.03 (0.006)	1.71E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg09199598	chr17: 3461480	<i>TRPV3</i>	0.022 (0.005)	1.68E-05	0.04	no	no	Open Sea	within 200 bp of TSS
cg11895950	chrX: 44732372	<i>KDM6A</i>	0.002 (0)	1.72E-05	0.04	no	no	Island	within 200 bp of TSS
cg14112754	chr3: 194118613	<i>GP5</i>	-0.039 (0.008)	1.70E-05	0.04	no	no	Island	within gene body
cg16170878	chr13: 49659276	<i>FNDC3A</i>	-0.035 (0.008)	1.70E-05	0.04	not tested	not tested	Open Sea	within gene body
cg18018385	chr10: 101964284	<i>CHUK</i>	0.016 (0.004)	1.72E-05	0.04	not tested	not tested	Open Sea	within gene body
cg26338757	chr10: 88428295	<i>LDB3</i>	-0.037 (0.008)	1.70E-05	0.04	no	no	Open Sea	within 200 bp of TSS
cg26915384	chr16: 27896619	<i>GSG1L</i>	-0.01 (0.002)	1.71E-05	0.04	no	no	Open Sea	within gene body
cg06835772	chr16: 85296220	NA	-0.035 (0.008)	1.76E-05	0.04	yes	no	Open Sea	
cg14827165	chr19: 17221420	<i>MYO9B</i>	-0.025 (0.005)	1.76E-05	0.04	not tested	not tested	Open Sea	within gene body
cg20170309	chr16: 50753273	<i>NOD2</i>	0.021 (0.005)	1.76E-05	0.04	not tested	not tested	Open Sea	within gene body
cg11170796	chr19: 1650224	<i>TCF3</i>	0.024 (0.005)	1.78E-05	0.04	no	no	South Shelf	within gene body
cg02202721	chr1: 156865043	<i>PEAR1</i>	-0.033 (0.007)	1.79E-05	0.04	not tested	not tested	South Shore	5'UTR
cg14425843	chr7: 92729833	<i>SAMD9</i>	0.012 (0.003)	1.79E-05	0.04	no	no	Open Sea	3'UTR
cg08319238	chr19: 45312525	<i>BCAM</i>	-0.025 (0.005)	1.82E-05	0.04	no	no	Open Sea	within gene body
cg11673291	chr1: 36787145	NA	-0.035 (0.008)	1.81E-05	0.04	no	no	South Shore	
cg22665096	chr12: 42102842	NA	-0.02 (0.004)	1.82E-05	0.04	no	no	Island	
cg24437293	chr19: 2065374	NA	0.027 (0.006)	1.83E-05	0.04	no	no	Open Sea	
cg22191973	chr18: 55292558	NA	0.021 (0.005)	1.84E-05	0.04	no	no	South Shore	
cg17885233	chr3: 132450221	<i>NPHP3-AS1</i>	-0.051 (0.011)	1.84E-05	0.04	not tested	not tested	South Shelf	within gene body
cg14396995	chr7: 42278089	<i>GLI3</i>	0.06 (0.013)	1.86E-05	0.04	no	no	Open Sea	within 1500 bp of TSS
cg04157263	chr17: 37752991	NA	-0.027 (0.006)	1.87E-05	0.04	no	no	South Shore	
cg07131742	chr11: 66112880	<i>B3GNT1</i>	-0.041 (0.009)	1.89E-05	0.04	no	no	Island	
cg12423902	chr6: 30159309	<i>TRIM26</i>	0.013 (0.003)	1.89E-05	0.04	no	no	North Shore	3'UTR
								Open Sea	within gene body

cg13962771	chr5: 140048068	<i>WDR55</i>	0.019 (0.004)	1.90E-05	0.04	not tested	not tested	South Shelf	within gene body
cg03917515	chr16: 53465339	NA	0.017 (0.004)	1.91E-05	0.04	no	no	North Shelf	
cg04552136	chr22: 50656153	<i>TUBGCP6</i>	0.02 (0.004)	1.91E-05	0.04	no	no	North Shore	3'UTR
cg05454781	chr1: 10651344	<i>PEX14</i>	-0.034 (0.007)	1.91E-05	0.04	not tested	not tested	Open Sea	within gene body
cg10142738	chr11: 19757625	<i>NAV2</i>	-0.035 (0.008)	1.93E-05	0.04	not tested	not tested	Open Sea	within gene body
cg15472784	chr1: 3663531	<i>KIAA0495</i>	-0.003 (0.001)	1.93E-05	0.04	no	no	in CpG Island	within 1st exon
cg21801962	chr1: 57602295	<i>DAB1</i>	0.02 (0.004)	1.94E-05	0.04	not tested	not tested	Open Sea	ExonBnd
cg01530448	chr21: 36319162	<i>RUNX1</i>	0.011 (0.003)	1.94E-05	0.04	not tested	not tested	Open Sea	within gene body
cg06596521	chr3: 126263868	<i>C3orf22</i>	-0.042 (0.009)	1.95E-05	0.04	not tested	not tested	South Shelf	within gene body
cg12836643	chr22: 39129370	<i>GTPBP1</i>	-0.03 (0.007)	1.95E-05	0.04	yes	yes	Open Sea	3'UTR
cg18073938	chr4: 100789493	<i>DAPP1</i>	-0.032 (0.007)	1.97E-05	0.04	not tested	not tested	Open Sea	3'UTR
cg21034201	chr18: 33160855	NA	-0.021 (0.005)	1.96E-05	0.04	not tested	not tested	North Shore	
cg21844291	chr2: 11097873	NA	-0.029 (0.006)	1.98E-05	0.04	no	no	North Shelf	
cg10058373	chr10: 120766572	NA	-0.032 (0.007)	2.00E-05	0.04	not tested	not tested	Open Sea	
cg27056175	chr8: 141556352	<i>EIF2C2</i>	0.006 (0.001)	2.01E-05	0.04	no	no	North Shelf	within gene body
cg00102795	chr10: 3151915	<i>PFKP</i>	0.017 (0.004)	2.05E-05	0.04	not tested	not tested	South Shelf	within gene body
cg15909006	chr16: 2086421	<i>SLC9A3R2</i>	0.026 (0.006)	2.06E-05	0.04	no	no	in CpG Island	within gene body
cg21886561	chr12: 53730326	<i>SP7</i>	-0.024 (0.005)	2.07E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg15187175	chr13: 94176949	<i>GPC6</i>	0.021 (0.005)	2.08E-05	0.04	no	no	Open Sea	within gene body
cg00441550	chr20: 29955998	<i>DEFB118</i>	-0.06 (0.013)	2.21E-05	0.04	not tested	not tested	Open Sea	within 1500 bp of TSS
cg01052743	chr8: 128747083	<i>MYC</i>	0.006 (0.001)	2.47E-05	0.04	no	no	North Shore	within 1500 bp of TSS
cg01260075	chr17: 28620354	<i>BLMH</i>	0.015 (0.003)	2.31E-05	0.04	not tested	not tested	South Shore	within 1500 bp of TSS
cg02147126	chr19: 827715	<i>AZU1</i>	-0.031 (0.007)	2.35E-05	0.04	no	no	Open Sea	within 200 bp of TSS
cg02956226	chr17: 4917032	<i>KIF1C</i>	0.016 (0.004)	2.19E-05	0.04	not tested	not tested	Open Sea	ExonBnd
cg03435866	chr2: 30452607	NA	0.009 (0.002)	2.28E-05	0.04	no	no	North Shore	
cg03520471	chr3: 97753623	<i>GABRR3</i>	-0.054 (0.012)	2.30E-05	0.04	no	no	Open Sea	within gene body
cg03678999	chr1: 1912135	<i>CFAP74</i>	0.023 (0.005)	2.47E-05	0.04	not tested	not tested	in CpG Island	within gene body

cg04708601	chr6: 101880078	<i>GRIK2</i>	-0.051 (0.011)	2.19E-05	0.04	no	no	Open Sea	within gene body
cg05002615	chr7: 68326108	NA	0.005 (0.001)	2.22E-05	0.04	no	no	Open Sea	
cg05233535	chr12: 6497969	<i>LTBR</i>	0.015 (0.003)	2.42E-05	0.04	not tested	not tested	Open Sea	within gene body
cg05293706	chr2: 219194675	<i>PNKD</i>	-0.036 (0.008)	2.24E-05	0.04	not tested	not tested	Open Sea	within gene body
cg05370277	chr4: 10006097	<i>SLC2A9</i>	0.019 (0.004)	2.12E-05	0.04	not tested	not tested	Open Sea	within gene body
cg05516255	chr15: 75652110	<i>MAN2C1</i>	0.023 (0.005)	2.38E-05	0.04	not tested	not tested	South Shelf	within gene body
cg05712904	chr19: 2692137	<i>GNG7</i>	0.023 (0.005)	2.46E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg05731156	chr16: 30418364	<i>ZNF771</i>	-0.01 (0.002)	2.28E-05	0.04	no	no	North Shore	within 1500 bp of TSS
cg05797982	chr5: 71764958	<i>ZNF366</i>	-0.041 (0.009)	2.19E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg05990312	chr17: 19628421	NA	-0.036 (0.008)	2.37E-05	0.04	no	no	South Shore	
cg07064050	chr19: 19165011	<i>ARMC6</i>	0.025 (0.006)	2.18E-05	0.04	no	no	Open Sea	within gene body
cg07126444	chr14: 75608010	<i>TMED10</i>	-0.047 (0.01)	2.34E-05	0.04	not tested	not tested	Open Sea	within gene body
cg07511317	chr14: 104159997	<i>KLC1</i>	0.014 (0.003)	2.47E-05	0.04	no	no	Open Sea	within gene body
cg08257567	chr3: 46009762	<i>FYCO1</i>	0.019 (0.004)	2.41E-05	0.04	not tested	not tested	Open Sea	within gene body
cg08343999	chr21: 43635188	<i>ABCG1</i>	0.019 (0.004)	2.26E-05	0.04	not tested	not tested	North Shelf	within 1500 bp of TSS
cg08743392	chr20: 33543028	<i>GSS</i>	-0.027 (0.006)	2.41E-05	0.04	no	no	North Shore	5'UTR
cg08811516	chr13: 35043968	<i>LINC00457</i>	-0.04 (0.009)	2.40E-05	0.04	not tested	not tested	Open Sea	within gene body
cg09023892	chr22: 38072101	<i>LGALS1</i>	-0.033 (0.007)	2.47E-05	0.04	not tested	not tested	North Shore	within gene body
cg09060489	chr1: 27874526	<i>AHDC1</i>	0.025 (0.006)	2.46E-05	0.04	no	no	in CpG Island	within gene body
cg09953898	chr2: 8935087	<i>KIDINS220</i>	-0.044 (0.01)	2.28E-05	0.04	not tested	not tested	Open Sea	within gene body
cg10370599	chr16: 22825158	<i>HS3ST2</i>	-0.004 (0.001)	2.40E-05	0.04	no	no	in CpG Island	within 1500 bp of TSS
cg11599849	chr1: 48809125	<i>SPATA6</i>	0.016 (0.003)	2.28E-05	0.04	not tested	not tested	Open Sea	within gene body
cg11980819	chr19: 4302579	<i>TMIGD2</i>	-0.026 (0.006)	2.22E-05	0.04	yes	no	North Shore	within 200 bp of TSS
cg12063619	chr13: 92868702	<i>GPC5</i>	-0.046 (0.01)	2.45E-05	0.04	not tested	not tested	Open Sea	within gene body
cg12249789	chr21: 45203404	NA	0.036 (0.008)	2.42E-05	0.04	yes	no	North Shelf	
cg12568707	chr19: 19042904	<i>HOMER3</i>	0.021 (0.005)	2.31E-05	0.04	no	no	in CpG Island	within gene body



cg12973855	chr15: 59816483	NA	-0.038 (0.008)	2.13E-05	0.04	not tested	not tested	Open Sea	
cg13657983	chr5: 73405407	NA	0.021 (0.005)	2.39E-05	0.04	not tested	not tested	Open Sea	
cg14153927	chr19: 46846465	<i>HIF3A</i>	-0.032 (0.007)	2.29E-05	0.04	no	no	North Shelf	3'UTR within 1500 bp of TSS
cg14374920	chr11: 57996779	<i>OR10Q1</i>	0.011 (0.003)	2.46E-05	0.04	not tested	not tested	Open Sea	
cg15059075	chr19: 30264378	NA	0.023 (0.005)	2.33E-05	0.04	not tested	not tested	Open Sea	
cg15235434	chr1: 171197048	NA	0.015 (0.003)	2.42E-05	0.04	not tested	not tested	Open Sea	
cg15701979	chr4: 20554680	<i>SLIT2</i>	0.024 (0.005)	2.46E-05	0.04	not tested	not tested	Open Sea	within gene body
cg16145176	chr21: 25596030	NA	-0.06 (0.013)	2.32E-05	0.04	not tested	not tested	Open Sea	
cg16350196	chr4: 137426420	NA	-0.052 (0.011)	2.36E-05	0.04	not tested	not tested	Open Sea	
cg16524284	chr19: 33353338	<i>SLC7A9</i>	0.027 (0.006)	2.15E-05	0.04	no	no	South Shelf	within gene body
cg16713094	chr9: 99450648	NA	0.021 (0.005)	2.14E-05	0.04	not tested	not tested	South Shore	
cg18713358	chr11: 67038249	<i>ADRBK1</i>	-0.028 (0.006)	2.26E-05	0.04	not tested	not tested	South Shelf	within gene body
cg19190900	chr2: 37553621	NA	0.053 (0.012)	2.23E-05	0.04	no	no	South Shore	
cg19194448	chr2: 178976361	<i>RBM45</i>	0.012 (0.003)	2.09E-05	0.04	no	no	North Shore	within 1500 bp of TSS
cg20142271	chr4: 81106287	<i>PRDM8</i>	-0.005 (0.001)	2.30E-05	0.04	no	no	South Shore	within 200 bp of TSS within gene body
cg20637770	chr1: 212872225	<i>BATF3</i>	-0.027 (0.006)	2.36E-05	0.04	not tested	not tested	North Shore	
cg20736045	chr8: 146270290	NA	-0.039 (0.009)	2.44E-05	0.04	not tested	not tested	Open Sea	
cg21016438	chr1: 109843435	<i>MYBPHL</i>	-0.031 (0.007)	2.44E-05	0.04	not tested	not tested	Open Sea	within gene body
cg21165486	chr1: 165606857	<i>MGST3</i>	-0.034 (0.008)	2.10E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg21386863	chr2: 150977022	NA	-0.04 (0.009)	2.23E-05	0.04	no	no	Open Sea	
cg21637741	chr8: 69834365	<i>LINC01592</i>	-0.052 (0.011)	2.40E-05	0.04	not tested	not tested	Open Sea	within gene body
cg21721331	chr1: 157670877	<i>FCRL3</i>	-0.061 (0.013)	2.13E-05	0.04	not tested	not tested	Open Sea	within 1500 bp of TSS
cg21806273	chr1: 247578953	<i>NLRP3</i>	-0.042 (0.009)	2.26E-05	0.04	no	no	Open Sea	within 1500 bp of TSS
cg22059430	chr7: 128346474	NA	0.014 (0.003)	2.14E-05	0.04	not tested	not tested	Open Sea	
cg22549504	chr19: 17448937	<i>GTPBP3</i>	0.001 (0)	2.29E-05	0.04	no	no	in CpG Island	within gene body within 200 bp of TSS
cg22574288	chr9: 22646113	<i>LINC01239</i>	-0.049 (0.011)	2.34E-05	0.04	not tested	not tested	Open Sea	
cg22589055	chr8: 86973512	NA	-0.037 (0.008)	2.27E-05	0.04	not tested	not tested	Open Sea	
cg22686259	chr16: 57984539	<i>CNGB1</i>	-0.034 (0.008)	2.43E-05	0.04	not tested	not tested	Open Sea	within gene body
cg23024158	chr10: 78011952	<i>C10orf11</i>	-0.051 (0.011)	2.36E-05	0.04	yes	no	Open Sea	within gene body

cg25038337	chr8: 141551653	<i>AGO2</i>	-0.017 (0.004)	2.42E-05	0.04	not tested	not tested	Open Sea	within gene body
cg25133376	chr7: 73392981	NA	-0.026 (0.006)	2.25E-05	0.04	no	no	Open Sea	
cg25467652	chr1: 11795976	<i>AGTRAP</i>	-0.034 (0.007)	2.29E-05	0.04	no	no	Open Sea in CpG Island	within 200 bp of TSS within gene body
cg26617588	chr10: 73398446	<i>CDH23</i>	-0.027 (0.006)	2.18E-05	0.04	not tested	not tested	Open Sea in CpG Island	within gene body
cg27496793	chr2: 46926433	<i>SOCS5</i>	0.029 (0.006)	2.21E-05	0.04	no	no	Open Sea in CpG Island	5'UTR within 1st exon
cg14483291	chr11: 17569007	<i>OTOG</i>	-0.042 (0.009)	2.49E-05	0.04	not tested	not tested	South Shelf in CpG Island	within gene body
cg16661234	chr17: 10541620	<i>MYH3</i>	-0.003 (0.001)	2.49E-05	0.04	no	no	Open Sea	within gene body
cg00596184	chr16: 69350052	<i>VPS4A</i>	0.029 (0.006)	2.59E-05	0.04	no	no	Open Sea	within gene body
cg01002322	chr2: 6872536	<i>LINC00487</i>	-0.045 (0.01)	2.56E-05	0.04	not tested	not tested	Open Sea	within gene body
cg01004862	chr16: 67249478	<i>LRRC29</i>	0.021 (0.005)	2.58E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg02395812	chr14: 105955879	<i>C14orf80</i>	-0.036 (0.008)	2.59E-05	0.04	no	no	North Shore	within 1500 bp of TSS within gene body
cg03333101	chr19: 12954349	<i>MAST1</i>	0.023 (0.005)	2.60E-05	0.04	yes	no	North Shelf	
cg03665051	chr22: 37569910	NA	-0.032 (0.007)	2.55E-05	0.04	not tested	not tested	Open Sea	
cg03882382	chr19: 4540065	<i>LRG1</i>	-0.036 (0.008)	2.57E-05	0.04	no	no	North Shelf	within 200 bp of TSS within gene body
cg06390790	chr17: 3654836	<i>ITGAE</i>	0.025 (0.006)	2.58E-05	0.04	yes	no	North Shelf	within gene body
cg07460883	chr11: 65378788	<i>MAP3K11</i>	-0.025 (0.006)	2.54E-05	0.04	not tested	not tested	South Shelf in CpG Island	within gene body
cg08839210	chr17: 27045048	<i>RAB34</i>	-0.027 (0.006)	2.51E-05	0.04	yes	no	Open Sea	within 200 bp of TSS within gene body
cg10126398	chr1: 162825937	<i>C1orf110</i>	0.022 (0.005)	2.51E-05	0.04	no	no	Open Sea	
cg11933019	chr11: 99291687	<i>CNTN5</i>	-0.04 (0.009)	2.57E-05	0.04	no	no	Open Sea	5'UTR
cg15992232	chr20: 59524596	NA	0.021 (0.005)	2.60E-05	0.04	not tested	not tested	Open Sea	
cg16103159	chr22: 26561575	NA	-0.049 (0.011)	2.56E-05	0.04	no	no	North Shelf	
cg16344173	chr7: 2158623	<i>MAD1L1</i>	0.028 (0.006)	2.53E-05	0.04	no	no	South Shelf	within gene body
cg18359017	chr11: 5538958	<i>UBQLNL</i>	-0.039 (0.009)	2.56E-05	0.04	not tested	not tested	Open Sea	within 1500 bp of TSS
cg20141502	chr16: 28922391	<i>RABEP2</i>	0.018 (0.004)	2.52E-05	0.04	not tested	not tested	Open Sea	ExonBnd
cg26387796	chr7: 150147927	<i>GIMAP8</i>	-0.011 (0.002)	2.60E-05	0.04	no	no	Open Sea in CpG Island	within 200 bp of TSS within gene body
cg01940336	chr19: 47935484	<i>SLC8A2</i>	0.022 (0.005)	2.62E-05	0.04	no	no	Open Sea in CpG Island	within gene body

cg26610808	chr10: 102046685	<i>BLOC1S2</i>	-0.039 (0.009)	2.62E-05	0.04	yes	no	South Shore	within 1500 bp of TSS
cg20788793	chr20: 3773402	NA	0.008 (0.002)	2.63E-05	0.04	no	no	North Shelf in CpG Island	
cg03839949	chr3: 128210541	<i>GATA2</i>	-0.023 (0.005)	2.66E-05	0.04	no	no	Open Sea	5'UTR within 1st exon
cg23241914	chr1: 161193393	<i>APOA2</i>	0.019 (0.004)	2.66E-05	0.04	no	no	Open Sea	within 1st exon
cg25944620	chr10: 75401315	<i>MYOZ1</i>	0.019 (0.004)	2.66E-05	0.04	no	no	Open Sea	within 1500 bp of TSS
cg08473663	chr17: 26695438	<i>SEBOX</i>	0.016 (0.004)	2.67E-05	0.04	no	no	North Shelf	within gene body
cg15591386	chr1: 76265299	<i>MSH4</i>	-0.054 (0.012)	2.67E-05	0.04	no	no	South Shelf	
cg10387848	chr18: 29757472	NA	-0.036 (0.008)	2.69E-05	0.04	not tested	not tested	Open Sea	
cg14426913	chr6: 6956252	NA	0.026 (0.006)	2.69E-05	0.04	no	no	Open Sea	
cg02938807	chr14: 63785523	<i>GPHB5</i>	-0.069 (0.015)	2.72E-05	0.04	no	no	Open Sea	within 1500 bp of TSS
cg04572631	chr3: 158565194	NA	-0.028 (0.006)	2.72E-05	0.04	not tested	not tested	Open Sea	
cg08491668	chr6: 32935236	<i>BRD2</i>	-0.03 (0.007)	2.72E-05	0.04	no	no	North Shore	within 1500 bp of TSS
cg09917488	chr19: 39635460	<i>PAK4</i>	-0.027 (0.006)	2.72E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg10420626	chr6: 43741154	<i>VEGFA</i>	-0.057 (0.013)	2.72E-05	0.04	not tested	not tested	South Shore	5'UTR within gene body
cg15850010	chr1: 170690670	<i>PRRX1</i>	-0.03 (0.007)	2.73E-05	0.04	not tested	not tested	Open Sea	within 200 bp of TSS
cg12463158	chr7: 150902745	<i>IQCA1L</i>	0.014 (0.003)	2.75E-05	0.04	not tested	not tested	South Shore	within gene body
cg00612202	chr7: 926974	<i>C7orf20</i>	0.024 (0.005)	2.79E-05	0.04	no	no	North Shelf	within gene body
cg00666124	chr2: 54756403	<i>RPL23AP32</i>	0.011 (0.002)	2.86E-05	0.04	no	no	Open Sea	within gene body
cg00770158	chr3: 57134628	<i>IL17RD</i>	-0.027 (0.006)	2.98E-05	0.04	no	no	South Shelf	within gene body
cg01035334	chr11: 117883077	NA	-0.033 (0.008)	3.15E-05	0.04	not tested	not tested	Open Sea	
cg01598569	chr11: 130500748	NA	-0.026 (0.006)	3.05E-05	0.04	not tested	not tested	Open Sea	
cg01619618	chr1: 23610607	<i>LINC01355</i>	-0.024 (0.005)	3.13E-05	0.04	not tested	not tested	Open Sea	within gene body
cg01658960	chr12: 132690570	<i>GALNT9</i>	-0.04 (0.009)	2.80E-05	0.04	no	no	in CpG Island	within gene body
cg02053339	chr22: 43088726	<i>A4GALT</i>	0.028 (0.006)	2.86E-05	0.04	no	no	North Shore	3'UTR
cg02078604	chr1: 8797440	<i>RERE</i>	-0.042 (0.009)	3.01E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg02081718	chr6: 88300968	<i>RARS2</i>	0.014 (0.003)	3.14E-05	0.04	not tested	not tested	South Shore	within 1500 bp of TSS

cg03140624	chr1: 235931377	<i>LYST</i>	-0.049 (0.011)	3.09E-05	0.04	no	no	Open Sea	within gene body
cg03529447	chr9: 133274183	<i>HMCN2</i>	0.019 (0.004)	3.13E-05	0.04	not tested	not tested	Open Sea	within gene body
cg03638795	chr11: 416499	<i>SIGIRR</i>	-0.04 (0.009)	3.06E-05	0.04	yes	yes	Open Sea in CpG Island	5'UTR
cg03665908	chr19: 17631991	<i>PGLS</i>	0.03 (0.007)	3.07E-05	0.04	no	no	Open Sea in CpG Island	3'UTR
cg04262465	chr14: 101405693	<i>SNORD113-6</i>	-0.039 (0.009)	2.91E-05	0.04	no	no	Open Sea	within 200 bp of TSS
cg04528240	chr4: 56504657	NA	-0.017 (0.004)	3.15E-05	0.04	no	no	South Shelf	
cg04609640	chr1: 45254092	<i>BEST4</i>	-0.035 (0.008)	3.15E-05	0.04	no	no	South Shore	within 1500 bp of TSS
cg04728045	chr11: 111298336	NA	-0.048 (0.011)	2.90E-05	0.04	not tested	not tested	Open Sea	
cg04742397	chr14: 95986554	NA	-0.034 (0.008)	2.82E-05	0.04	yes	no	South Shelf	
cg05094137	chr16: 53125208	<i>CHD9</i>	-0.028 (0.006)	3.14E-05	0.04	no	no	Open Sea	5'UTR
cg05256584	chr2: 40452795	<i>SLC8A1</i>	0.021 (0.005)	3.03E-05	0.04	no	no	Open Sea	within gene body
cg06525670	chr13: 30528708	NA	-0.041 (0.009)	2.93E-05	0.04	no	no	Open Sea	
cg06823863	chr16: 19296692	<i>LOC728276</i>	0.013 (0.003)	2.88E-05	0.04	no	no	Open Sea	within 1500 bp of TSS
cg06887251	chr5: 67576008	<i>PIK3R1</i>	-0.054 (0.012)	2.83E-05	0.04	not tested	not tested	Open Sea	within gene body
cg06923291	chr12: 90456743	NA	-0.038 (0.008)	2.97E-05	0.04	not tested	not tested	Open Sea	
cg07666998	chr4: 8254585	NA	-0.04 (0.009)	3.07E-05	0.04	not tested	not tested	Open Sea	
cg08202553	chr19: 36156064	<i>UPK1A</i>	0.013 (0.003)	3.13E-05	0.04	not tested	not tested	Open Sea	within 1500 bp of TSS
cg08301307	chr14: 103599204	<i>TNFAIP2</i>	0.019 (0.004)	2.90E-05	0.04	no	no	Open Sea	within gene body
cg08450168	chr1: 28918231	<i>RAB42</i>	0.02 (0.005)	2.84E-05	0.04	no	no	North Shore	within 1500 bp of TSS
cg09427273	chr10: 11077625	<i>CUGBP2</i>	-0.028 (0.006)	3.16E-05	0.04	no	no	Open Sea	within gene body
cg09780594	chr9: 96576175	NA	-0.032 (0.007)	3.08E-05	0.04	not tested	not tested	Open Sea	
cg10153638	chr3: 156835317	<i>LINC00880</i>	-0.044 (0.01)	3.15E-05	0.04	not tested	not tested	North Shelf	within gene body
cg10232265	chr10: 126782326	<i>CTBP2</i>	0.026 (0.006)	2.83E-05	0.04	no	no	Open Sea	5'UTR
cg10428881	chr14: 81770194	<i>STON2</i>	-0.036 (0.008)	3.11E-05	0.04	not tested	not tested	Open Sea	within gene body
cg10698419	chr4: 72897317	<i>NPFFR2</i>	0.021 (0.005)	3.11E-05	0.04	no	no	North Shore	within 1500 bp of TSS
cg11579421	chr10: 134211857	<i>PWWP2B</i>	-0.041 (0.009)	3.02E-05	0.04	no	no	South Shore	within gene body

cg11902424	chr5: 2252995	NA	0.043 (0.01)	3.11E-05	0.04	no	no	Open Sea	
cg12157761	chr15: 71005778	<i>UACA</i>	-0.039 (0.009)	2.99E-05	0.04	no	no	Open Sea	within gene body
cg12234652	chr19: 35811489	NA	-0.026 (0.006)	3.14E-05	0.04	not tested	not tested	Open Sea	
cg12891543	chr16: 53958626	<i>FTO</i>	-0.052 (0.012)	3.09E-05	0.04	not tested	not tested	Open Sea	within gene body
cg13092082	chr1: 192602520	NA	-0.025 (0.006)	3.02E-05	0.04	no	no	Open Sea	
cg13131168	chr8: 145542119	<i>DGAT1</i>	0.024 (0.005)	3.16E-05	0.04	not tested	not tested	Open Sea	within gene body
cg13537774	chr9: 84088338	NA	0.016 (0.004)	2.91E-05	0.04	no	no	Open Sea	
cg13645530	chr12: 116756948	NA	-0.045 (0.01)	3.14E-05	0.04	yes	yes	Open Sea	
cg15047616	chr22: 27015719	NA	-0.031 (0.007)	2.86E-05	0.04	not tested	not tested	Open Sea	
cg15156528	chr12: 49583981	<i>TUBA1A</i>	-0.037 (0.008)	3.12E-05	0.04	not tested	not tested	South Shore	within 1500 bp of TSS
cg15221794	chr13: 29943389	<i>MTUS2</i>	-0.005 (0.001)	3.10E-05	0.04	not tested	not tested	Open Sea	within gene body
cg15616051	chr3: 122770795	NA	-0.026 (0.006)	2.81E-05	0.04	not tested	not tested	Open Sea	
cg17594681	chr19: 45991739	<i>RTN2</i>	0.024 (0.005)	3.09E-05	0.04	not tested	not tested	Open Sea	within gene body
cg17704620	chr14: 77763369	<i>POMT2</i>	0.014 (0.003)	3.01E-05	0.04	not tested	not tested	Open Sea	within gene body
cg17712081	chr12: 57662315	<i>R3HDM2</i>	-0.024 (0.005)	3.13E-05	0.04	not tested	not tested	Open Sea	within gene body
cg17844178	chr16: 12562911	<i>SNX29</i>	0.009 (0.002)	2.87E-05	0.04	not tested	not tested	Open Sea	within gene body
cg18064897	chrX: 10085184	<i>WWC3</i>	0.028 (0.006)	3.09E-05	0.04	no	no	in CpG Island	within gene body
cg18215449	chr12: 66089473	NA	-0.045 (0.01)	2.90E-05	0.04	no	no	Open Sea	
cg18308901	chr9: 140376822	<i>PNPLA7</i>	-0.028 (0.006)	2.82E-05	0.04	not tested	not tested	South Shore	within gene body
cg18681014	chr14: 105660876	NA	-0.04 (0.009)	3.07E-05	0.04	no	no	North Shore	
cg20300412	chr4: 65749341	NA	-0.064 (0.014)	3.07E-05	0.04	not tested	not tested	Open Sea	
cg20302236	chr8: 28637293	<i>INTS9</i>	-0.028 (0.006)	3.07E-05	0.04	not tested	not tested	Open Sea	within gene body
cg20653075	chr8: 65291682	<i>MIR124-2</i>	-0.024 (0.005)	2.97E-05	0.04	no	no	South Shore	within 200 bp of TSS
cg21359538	chr4: 76440740	<i>RCHY1</i>	-0.062 (0.014)	3.05E-05	0.04	not tested	not tested	South Shore	within 1500 bp of TSS
cg21452013	chr3: 31269300	NA	0.009 (0.002)	2.82E-05	0.04	not tested	not tested	Open Sea	
cg21784411	chr1: 3251502	<i>PRDM16</i>	0.025 (0.006)	2.88E-05	0.04	yes	no	Open Sea	within gene body
cg22239593	chr10: 103540102	<i>FGF8</i>	-0.028 (0.006)	3.06E-05	0.04	not tested	not tested	South Shore	5'UTR
cg22265441	chr15: 58011290	NA	0.013 (0.003)	2.79E-05	0.04	not tested	not tested	Open Sea	

cg22848722	chr10: 80917822	<i>ZMIZ1</i>	-0.037 (0.008)	2.88E-05	0.04	not tested	not tested	Open Sea	5'UTR
cg25921418	chr6: 31621008	<i>BAT3</i>	-0.009 (0.002)	2.99E-05	0.04	no	no	in CpG Island	within 1500 bp of TSS
cg26431261	chr8: 74418384	<i>STAU2</i>	0.017 (0.004)	3.12E-05	0.04	not tested	not tested	Open Sea	within gene body
cg24907814	chr5: 2758088	NA	-0.028 (0.006)	3.17E-05	0.04	no	no	South Shore	
cg06794088	chr19: 19426589	<i>SUGP1</i>	0.026 (0.006)	3.17E-05	0.04	not tested	not tested	Open Sea	within gene body
cg09732711	chr10: 130696072	NA	-0.03 (0.007)	3.18E-05	0.04	no	no	Open Sea	
cg20493821	chr15: 89341999	NA	-0.024 (0.005)	3.21E-05	0.04	not tested	not tested	Open Sea	
cg21688288	chr21: 44181258	<i>PDE9A</i>	0.022 (0.005)	3.22E-05	0.04	no	no	Open Sea in CpG Island	within gene body
cg06168449	chr19: 38714549	<i>DPF1</i>	0.018 (0.004)	3.26E-05	0.05	no	no	Open Sea	within gene body
cg11764535	chr6: 46380623	<i>RCAN2</i>	-0.04 (0.009)	3.25E-05	0.05	not tested	not tested	Open Sea	within gene body
cg01772854	chr5: 1176225	NA	0.031 (0.007)	3.28E-05	0.05	no	no	Open Sea	
cg02329351	chr13: 44977492	<i>TUSC8</i>	-0.019 (0.004)	3.37E-05	0.05	not tested	not tested	Open Sea	within gene body
cg02966624	chr1: 150668227	<i>GOLPH3L</i>	-0.037 (0.008)	3.33E-05	0.05	not tested	not tested	Open Sea	5'UTR
cg03457781	chr3: 20418856	NA	-0.021 (0.005)	3.31E-05	0.05	no	no	Open Sea	
cg04823228	chr5: 176258443	<i>UNC5A</i>	0.024 (0.005)	3.40E-05	0.05	not tested	not tested	Open Sea	within gene body
cg06549111	chr12: 58287804	NA	-0.025 (0.006)	3.39E-05	0.05	not tested	not tested	North Shelf	
cg06679537	chr9: 112210147	<i>PTPN3</i>	-0.027 (0.006)	3.29E-05	0.05	not tested	not tested	Open Sea	within gene body
cg08410015	chr10: 119862094	<i>CASC2</i>	-0.035 (0.008)	3.33E-05	0.05	not tested	not tested	Open Sea in CpG Island	within gene body
cg12817436	chr19: 1068561	<i>HMHA1</i>	-0.023 (0.005)	3.36E-05	0.05	no	no	Open Sea	within 1500 bp of TSS
cg13590419	chr20: 43209782	<i>PKIG</i>	-0.035 (0.008)	3.39E-05	0.05	not tested	not tested	Open Sea	
cg14080033	chr7: 2663085	NA	-0.029 (0.007)	3.40E-05	0.05	not tested	not tested	Open Sea	
cg16994421	chr17: 33569462	<i>SLFN5</i>	-0.005 (0.001)	3.40E-05	0.05	not tested	not tested	in CpG Island	within 1500 bp of TSS
cg18388619	chr17: 1792197	<i>RPA1</i>	0.021 (0.005)	3.36E-05	0.05	no	no	Open Sea	within gene body
cg18841746	chr4: 114681688	<i>CAMK2D</i>	0.005 (0.001)	3.38E-05	0.05	no	no	North Shore	within gene body
cg18964464	chr12: 93741046	<i>LOC643339</i>	-0.031 (0.007)	3.37E-05	0.05	not tested	not tested	Open Sea	within gene body
cg19008646	chr3: 31145476	NA	-0.019 (0.004)	3.33E-05	0.05	no	no	Open Sea	
cg20781421	chr11: 11866554	<i>USP47</i>	-0.033 (0.007)	3.37E-05	0.05	no	no	South Shelf	within gene body

cg23502495	chr16: 3175677	<i>ZNF213-AS1</i>	0.012 (0.003)	3.31E-05	0.05	not tested	not tested	South Shore	within gene body
cg24743838	chr8: 143696464	<i>ARC</i>	-0.029 (0.007)	3.30E-05	0.05	not tested	not tested	South Shore	within 1500 bp of TSS
cg25139718	chr1: 2027575	<i>PRKCZ</i>	0.021 (0.005)	3.37E-05	0.05	no	no	South Shore	within gene body
cg27160460	chr11: 66617512	<i>PC</i>	0.024 (0.005)	3.36E-05	0.05	not tested	not tested	Open Sea	within gene body
cg27509293	chr6: 14919597	NA	-0.057 (0.013)	3.36E-05	0.05	not tested	not tested	Open Sea	
cg00325007	chr9: 5774228	<i>RIC1</i>	0.013 (0.003)	3.41E-05	0.05	not tested	not tested	Open Sea	within gene body
cg07887517	chr17: 79005277	<i>BAIAP2-AS1</i>	-0.034 (0.008)	3.45E-05	0.05	not tested	not tested	North Shore	within gene body
cg11531968	chr4: 73969865	<i>ANKRD17</i>	0.016 (0.004)	3.44E-05	0.05	not tested	not tested	Open Sea	within gene body
cg12342178	chr1: 238282400	NA	-0.022 (0.005)	3.44E-05	0.05	not tested	not tested	Open Sea	
cg11845488	chr14: 70189638	NA	0.011 (0.002)	3.46E-05	0.05	no	no	North Shelf	
cg14293102	chr19: 2232170	<i>DOT1L</i>	0.011 (0.003)	3.47E-05	0.05	no	no	South Shore	3'UTR
cg01370074	chr3: 170902250	<i>TNIK</i>	-0.04 (0.009)	3.53E-05	0.05	not tested	not tested	Open Sea	within gene body
cg10684056	chr8: 128494566	<i>CASC8</i>	-0.022 (0.005)	3.53E-05	0.05	not tested	not tested	Open Sea	within 200 bp of TSS
cg19995259	chr19: 53795827	<i>BIRC8</i>	-0.056 (0.013)	3.53E-05	0.05	not tested	not tested	South Shore	within 1500 bp of TSS
cg23178580	chr11: 6806121	<i>OR2AG1</i>	-0.022 (0.005)	3.53E-05	0.05	not tested	not tested	Open Sea	within 200 bp of TSS
cg26723045	chr11: 9042581	<i>SCUBE2</i>	-0.027 (0.006)	3.52E-05	0.05	no	no	Open Sea	3'UTR
cg10007431	chr14: 89866249	<i>FOXN3</i>	-0.044 (0.01)	3.57E-05	0.05	not tested	not tested	Open Sea	within gene body
cg15988812	chr19: 33889481	<i>PEPD</i>	0.026 (0.006)	3.57E-05	0.05	no	no	North Shelf	within gene body
cg24996724	chr16: 2286426	<i>DNASE1L2</i>	-0.028 (0.006)	3.56E-05	0.05	not tested	not tested	South Shore	within 200 bp of TSS
cg00453272	chr10: 76574026	NA	0.017 (0.004)	3.63E-05	0.05	no	no	South Shore	
cg01362696	chr10: 63348729	NA	-0.031 (0.007)	3.61E-05	0.05	not tested	not tested	Open Sea	
cg07160014	chr11: 47959926	NA	-0.04 (0.009)	3.63E-05	0.05	no	no	Open Sea	
cg09352336	chr6: 3410628	<i>SLC22A23</i>	0.019 (0.004)	3.63E-05	0.05	not tested	not tested	Open Sea	5'UTR
cg10493330	chr5: 179709813	<i>MAPK9</i>	0.015 (0.003)	3.63E-05	0.05	no	no	Open Sea	5'UTR
cg14456982	chr17: 17074142	<i>MPRIP</i>	0.016 (0.004)	3.62E-05	0.05	not tested	not tested	Open Sea	within gene body
cg16840609	chr15: 51397257	<i>TNFAIP8L3</i>	-0.034 (0.008)	3.63E-05	0.05	not tested	not tested	Open Sea	within 1st exon
cg24130603	chr1: 161062428	NA	0.009 (0.002)	3.58E-05	0.05	not tested	not tested	Open Sea	
cg24430703	chr7: 55621681	<i>VOPPI</i>	0.021 (0.005)	3.62E-05	0.05	no	no	Open Sea	within gene body

cg27253783	chr10: 14338581	<i>FRMD4A</i>	0.007 (0.002)	3.61E-05	0.05	not tested	not tested	Open Sea	within gene body
cg11539188	chr10: 3170957	<i>PFKP</i>	0.023 (0.005)	3.64E-05	0.05	not tested	not tested	Open Sea	within gene body
cg12278739	chr11: 68795647	NA	-0.028 (0.006)	3.65E-05	0.05	not tested	not tested	Open Sea	
cg00885708	chr5: 139167076	NA	-0.025 (0.006)	3.69E-05	0.05	no	no	North Shore	
cg06030722	chr6: 127568996	NA	0.01 (0.002)	3.69E-05	0.05	not tested	not tested	Open Sea	
cg11682700	chr3: 114477956	<i>ZBTB20</i>	0.013 (0.003)	3.68E-05	0.05	not tested	not tested	Open Sea	within 1st exon
cg06680529	chr17: 79920755	NA	0.027 (0.006)	3.72E-05	0.05	no	no	Open Sea	in CpG Island
cg04422752	chr10: 102028175	<i>CWF19L1</i>	0.011 (0.002)	3.74E-05	0.05	not tested	not tested	South Shore	within 1500 bp of TSS
cg13705180	chr7: 31978680	<i>PDE1C</i>	0.012 (0.003)	3.74E-05	0.05	not tested	not tested	Open Sea	within gene body
cg07771893	chr16: 27188676	NA	0.015 (0.003)	3.77E-05	0.05	not tested	not tested	Open Sea	
cg18548615	chr17: 32295722	<i>ASIC2</i>	-0.013 (0.003)	3.78E-05	0.05	not tested	not tested	Open Sea	within gene body
cg20779373	chr1: 37428969	<i>GRIK3</i>	-0.035 (0.008)	3.77E-05	0.05	no	no	Open Sea	within gene body
cg25133753	chr20: 44299726	<i>WFDC11</i>	-0.039 (0.009)	3.78E-05	0.05	no	no	Open Sea	within 1500 bp of TSS
cg00367499	chr5: 170634447	<i>RANBP17</i>	0.062 (0.014)	3.81E-05	0.05	not tested	not tested	Open Sea	within gene body
cg01479664	chr16: 58016655	<i>TEPP</i>	0.036 (0.008)	3.81E-05	0.05	no	no	Open Sea	within gene body
cg24409539	chr2: 114034595	<i>PAX8</i>	-0.03 (0.007)	3.81E-05	0.05	no	no	Open Sea	in CpG Island
cg23291484	chr3: 150067838	NA	0.015 (0.003)	3.84E-05	0.05	not tested	not tested	Open Sea	
cg00244312	chr2: 131622518	NA	-0.025 (0.006)	3.86E-05	0.05	not tested	not tested	Open Sea	
cg01447564	chr5: 131335786	<i>ACSL6</i>	-0.042 (0.009)	3.88E-05	0.05	not tested	not tested	Open Sea	within gene body
cg12660171	chr17: 2026359	<i>SMG6</i>	-0.029 (0.007)	3.88E-05	0.05	not tested	not tested	Open Sea	within gene body
cg17258765	chr1: 25202617	NA	0.024 (0.005)	3.86E-05	0.05	not tested	not tested	Open Sea	
cg23978004	chr4: 142144530	<i>ZNF330</i>	0.017 (0.004)	3.88E-05	0.05	no	no	South Shelf	within gene body
cg09012071	chr19: 2171984	<i>DOT1L</i>	-0.027 (0.006)	3.93E-05	0.05	not tested	not tested	Open Sea	within gene body
cg13698574	chr2: 106364714	<i>NCK2</i>	-0.033 (0.008)	3.91E-05	0.05	not tested	not tested	South Shelf	5'UTR
cg14637909	chr10: 103618712	<i>C10orf76</i>	-0.04 (0.009)	3.91E-05	0.05	not tested	not tested	Open Sea	within gene body
cg16294620	chr20: 13280181	<i>ISM1</i>	0.021 (0.005)	3.91E-05	0.05	no	no	South Shore	3'UTR
cg26060224	chr1: 173604924	<i>ANKRD45</i>	0.031 (0.007)	3.92E-05	0.05	not tested	not tested	Open Sea	within gene body
cg26336118	chr1: 97303097	NA	0.008 (0.002)	3.89E-05	0.05	no	no	Open Sea	



cg27010208	chr11: 93263413	<i>SMCO4</i>	-0.03 (0.007)	3.91E-05	0.05	not tested	not tested	Open Sea	5'UTR
cg12434712	chr4: 40005867	NA	0.024 (0.006)	3.94E-05	0.05	not tested	not tested	Open Sea	
cg02998837	chr3: 168619603	<i>LOC100507661</i>	-0.024 (0.006)	4.01E-05	0.05	not tested	not tested	Open Sea	within 200 bp of TSS
cg10217365	chr19: 12890523	NA	-0.031 (0.007)	4.04E-05	0.05	not tested	not tested	South Shore	
cg10473700	chr11: 62359899	<i>TUT1</i>	-0.03 (0.007)	3.98E-05	0.05	not tested	not tested	South Shore	within 1500 bp of TSS
cg11485152	chr3: 3171664	<i>TRNT1</i>	-0.034 (0.008)	3.99E-05	0.05	no	no	South Shelf	within gene body
cg13977520	chr2: 158543191	NA	-0.032 (0.007)	3.98E-05	0.05	not tested	not tested	Open Sea	
cg14200834	chr19: 4278055	<i>SHD</i>	-0.029 (0.007)	3.97E-05	0.05	yes	no	North Shore	within 1500 bp of TSS
cg16521773	chr11: 865988	<i>TSPAN4</i>	0.026 (0.006)	4.01E-05	0.05	no	no	Open Sea	within gene body
cg17178175	chr2: 178109973	<i>NFE2L2</i>	-0.048 (0.011)	4.03E-05	0.05	no	no	Open Sea	within gene body
cg17540831	chr19: 4535992	<i>PLIN5</i>	0.026 (0.006)	4.03E-05	0.05	not tested	not tested	South Shore	within 1500 bp of TSS
cg17754042	chr4: 2338980	<i>ZFYVE28</i>	0.022 (0.005)	3.99E-05	0.05	no	no	North Shelf	within gene body
cg18781031	chr5: 127598507	<i>FBN2</i>	-0.039 (0.009)	3.97E-05	0.05	no	no	Open Sea	within gene body
cg20389995	chr21: 44462317	NA	0.026 (0.006)	4.01E-05	0.05	not tested	not tested	Open Sea	
cg22503060	chr12: 92368774	NA	0.013 (0.003)	3.98E-05	0.05	no	no	Open Sea	
cg22999603	chr11: 119537405	<i>PVRL1</i>	-0.031 (0.007)	3.97E-05	0.05	no	no	South Shore	within gene body
cg24208718	chr1: 212629727	NA	-0.047 (0.011)	4.02E-05	0.05	not tested	not tested	Open Sea	
cg00238899	chr10: 112046866	<i>MXI1</i>	0.013 (0.003)	4.05E-05	0.05	no	no	Open Sea	3'UTR
cg25463683	chr1: 55542596	<i>USP24</i>	-0.02 (0.005)	4.06E-05	0.05	not tested	not tested	Open Sea	within gene body
cg02172658	chr11: 2440093	<i>TRPM5</i>	0.035 (0.008)	4.20E-05	0.05	not tested	not tested	North Shore	within gene body
cg02257445	chr17: 14117857	NA	-0.045 (0.01)	4.12E-05	0.05	not tested	not tested	Open Sea	
cg02862505	chr12: 114939167	NA	0.011 (0.003)	4.14E-05	0.05	no	no	Open Sea	
cg03048947	chr1: 225611366	<i>LBR</i>	-0.045 (0.01)	4.17E-05	0.05	no	no	North Shelf	within gene body
cg04245616	chr15: 59543693	<i>MYO1E</i>	-0.072 (0.017)	4.20E-05	0.05	not tested	not tested	Open Sea	within gene body
cg04399598	chr21: 43956068	<i>SLC37A1</i>	-0.034 (0.008)	4.11E-05	0.05	not tested	not tested	Open Sea	within gene body
cg05075015	chr2: 216317679	<i>LOC102724849</i>	-0.021 (0.005)	4.18E-05	0.05	not tested	not tested	Open Sea	within 1500 bp of TSS

cg05875486	chr11: 655245	<i>DEAF1</i>	0.017 (0.004)	4.17E-05	0.05	not tested	not tested	Open Sea	within gene body
cg06820907	chr2: 242122206	<i>PPP1R7</i>	-0.002 (0)	4.15E-05	0.05	no	no	Open Sea	within gene body
cg08690174	chr6: 123959721	<i>TRDN</i>	-0.046 (0.011)	4.18E-05	0.05	not tested	not tested	Open Sea	within 1500 bp of TSS
cg11014079	chr7: 149517605	<i>SSPO</i>	-0.02 (0.005)	4.15E-05	0.05	no	no	Open Sea	within gene body
cg18024141	chr6: 152232729	<i>ESR1</i>	-0.029 (0.007)	4.11E-05	0.05	not tested	not tested	Open Sea	within gene body
cg18049487	chr19: 40709597	<i>MAP3K10</i>	0.017 (0.004)	4.14E-05	0.05	not tested	not tested	North Shelf	within gene body
cg19361399	chr2: 67405276	<i>LOC102800447</i>	0.035 (0.008)	4.12E-05	0.05	not tested	not tested	Open Sea	within gene body
cg21995472	chr12: 85271218	<i>SLC6A15</i>	-0.047 (0.011)	4.13E-05	0.05	not tested	not tested	Open Sea	within gene body
cg22393541	chr12: 11081043	<i>PRH2</i>	0.01 (0.002)	4.08E-05	0.05	not tested	not tested	Open Sea	within 1500 bp of TSS
cg24948374	chr20: 62869833	<i>MYT1</i>	-0.024 (0.006)	4.21E-05	0.05	not tested	not tested	Open Sea	within gene body
cg25221207	chr11: 119555633	<i>PVRL1</i>	-0.026 (0.006)	4.10E-05	0.05	no	no	Open Sea	within gene body
cg25506287	chr6: 26247955	<i>HIST1H4G</i>	0.009 (0.002)	4.14E-05	0.05	not tested	not tested	South Shore	within 1500 bp of TSS
cg26351916	chr17: 78084228	<i>GAA</i>	0.024 (0.005)	4.17E-05	0.05	no	no	South Shore	within gene body
cg27209994	chr18: 51750371	<i>MBD2</i>	0.007 (0.002)	4.09E-05	0.05	no	no	North Shore	within gene body
cg27399052	chr1: 1293868	<i>MXRA8</i>	-0.025 (0.006)	4.20E-05	0.05	no	no	South Shelf in CpG Island	within 1st exon
cg20478080	chr22: 45133246	<i>PRR5</i>	0.023 (0.005)	4.22E-05	0.05	no	no	Open Sea	3'UTR within gene body
cg05214676	chr4: 141005085	<i>MAML3</i>	0.031 (0.007)	4.25E-05	0.05	no	no	Open Sea	
cg00693782	chr11: 11097882	NA	-0.041 (0.009)	4.29E-05	0.05	not tested	not tested	Open Sea	
cg26686150	chr12: 93637466	NA	-0.026 (0.006)	4.29E-05	0.05	no	no	Open Sea	
cg06177446	chr20: 1093802	<i>PSMF1</i>	0.02 (0.005)	4.31E-05	0.05	no	no	Open Sea	within 200 bp of TSS
cg04394031	chr11: 65416901	<i>SIPA1</i>	0.025 (0.006)	4.33E-05	0.05	no	no	South Shore	within gene body
cg14540181	chr7: 7330669	NA	0.029 (0.007)	4.33E-05	0.05	not tested	not tested	Open Sea	
cg17463863	chr3: 139106943	<i>COPB2</i>	0.022 (0.005)	4.32E-05	0.05	not tested	not tested	North Shore	within gene body
cg18815657	chr5: 74130379	<i>FAM169A</i>	-0.03 (0.007)	4.34E-05	0.05	not tested	not tested	Open Sea	within gene body
cg23718496	chr19: 47875594	<i>DHX34</i>	0.018 (0.004)	4.38E-05	0.05	not tested	not tested	Open Sea	within gene body

cg17064521	chr15: 45740423	NA	-0.023 (0.005)	4.40E-05	0.05	not tested	not tested	Open Sea	
cg01047262	chr8: 38007025	<i>STAR</i>	-0.017 (0.004)	4.47E-05	0.05	not tested	not tested	Open Sea	within gene
cg01276573	chr17: 28672068	NA	-0.027 (0.006)	4.45E-05	0.05	not tested	not tested	Open Sea	body
cg02649474	chr16: 30673103	<i>FBRS</i>	0.02 (0.005)	4.48E-05	0.05	not tested	not tested	South Shore	within gene
cg06039201	chr3: 50737816	<i>DOCK3</i>	0.013 (0.003)	4.45E-05	0.05	not tested	not tested	Open Sea	body
cg06540015	chr1: 32203668	<i>ADGRB2</i>	0.024 (0.006)	4.42E-05	0.05	not tested	not tested	Open Sea	within gene
cg07092838	chr17: 72248179	<i>TTYH2</i>	0.024 (0.005)	4.48E-05	0.05	not tested	not tested	Open Sea	body
cg13176608	chr1: 204542634	NA	0.027 (0.006)	4.46E-05	0.05	not tested	not tested	Open Sea	
cg19989663	chr7: 115981565	NA	-0.056 (0.013)	4.46E-05	0.05	not tested	not tested	Open Sea	
cg20181240	chr1: 4029800	NA	-0.049 (0.011)	4.44E-05	0.05	not tested	not tested	Open Sea	
cg20335206	chr12: 120802252	<i>MSI1</i>	0.021 (0.005)	4.45E-05	0.05	no	no	North Shelf	within gene body

<sup>a</sup> Genomic location is according to genome build GRCh37/hg19

<sup>b</sup> Effect estimates represent the proportion of methylation difference at follow-up compared to baseline, adjusted for batch, cell type estimates, Hispanic ethnicity, estimated smoking pack-years, and a random intercept for individual to account for the repeated sampling design.

<sup>c</sup> Was this CpG site statistically significantly different when comparing current (or former) adult smokers to adults who never smoked? Comparing from the meta-analysis of ~16,000 adults published in Joehanes et al. 2016 *Circ Cardiovas Genetics* 9(5):436-447. Joehanes et al. used the 450K; 'not tested' sites were not included on that version of the Infinium array.

<sup>d</sup> Location of CpG site relative to a CpG Island

<sup>e</sup> Location of CpG site relative to nearest gene according to annotations from UCSC RefGene

**Supplemental Table S2. Difference in DNA methylation between baseline and follow-up at CpG sites Previously associated with firefighting**

Probe ID <sup>a</sup>	Genomic Location <sup>b</sup>	Gene Name	Estimate (SE) <sup>c</sup>	p-value
cg15304928	chr1: 201123562	<i>TMEM9</i>	-0.001 (0.002)	0.632
cg00287370	chr1: 234736092	NA	0.009 (0.004)	<b>0.009</b>
cg02932780	chr6: 31762353	<i>VAR5</i>	-0.005 (0.007)	0.541
cg09544149	chr10: 80588828	NA	-0.048 (0.016)	<b>0.004</b>
cg05236728	chr12: 47609513	<i>PCED1B-AS1</i>	0.001 (0.001)	0.309
cg03177084	chr17: 40985069	<i>PSME3</i>	0.002 (0.003)	0.535
cg22433210	chr17: 43662623	NA	-0.001 (0)	<b>0.031</b>
cg13753209	chr17: 57696993	<i>CLTC</i>	0 (0)	0.718
cg22280238	chr17: 79251323	<i>SLC38A10</i>	-0.001 (0.001)	0.197
cg07897354	chr18: 12657909	<i>SPIRE1</i>	0 (0)	0.280
cg20821958	chr19: 48614116	<i>PLA2G4C</i>	0.002 (0.001)	<b>0.007</b>
cg12253469	chr22: 37420454	<i>MPST</i>	-0.008 (0.015)	0.575
cg24034992	chrX: 67719066	<i>YIPF6</i>	-0.001 (0.006)	0.817

<sup>a</sup> Only CpG sites that differed when comparing new recruits and incumbent firefighters or associated with years in the service are included in this table, from Zhou et al. 2019

<sup>b</sup> Genomic location is according to genome build GRCh37/hg19

<sup>c</sup> Effect estimates represent the proportion of methylation difference at follow-up compared to baseline, adjusted for batch, cell type estimates, Hispanic ethnicity, estimated smoking pack-years, and a random intercept for individual to account for the repeated sampling.

NA means the CpG site is not within a gene or within a known feature (e.g. promoter) of a specific gene.

**Supplemental Table S3. Enriched gene sets annotated to disease and disease-related functions in IPA among differentially methylated genes comparing baseline to follow-up ( $q < 0.05$ )**

Broader Category of Disease	Gene-Set (Disease or Functional Annotation)	q-value for enrichment	# Differentially Methylated Genes in the gene-set
Cancer, Cell Cycle, Organismal Injury and Abnormalities	Interphase of cancer cells	0.030	4
	Arrest in interphase of cancer cells	0.035	3
	Arrest in G2 phase of cancer cells	0.044	2
Cancer, Dermatological Diseases and Conditions, Organismal Injury and Abnormalities	Skin cancer	0.048	242
	Pancreatic tumor	0.020	100
Cancer, Endocrine System Disorders, Gastrointestinal Disease, Organismal Injury and Abnormalities	Pancreatic cancer	0.035	88
	Pancreatic carcinoma	0.042	84
	Pancreatic adenocarcinoma	0.042	80
	Pancreatic ductal adenocarcinoma	0.044	78
	Large intestine adenocarcinoma	0.001	277
Cancer, Gastrointestinal Disease, Organismal Injury and Abnormalities	Large intestine neoplasm	0.001	283
	Malignant neoplasm of large intestine	0.001	282
	Colon tumor	0.001	178
	Gastrointestinal adenocarcinoma	0.001	280
	Stomach tumor	0.001	141
	Gastrointestinal carcinoma	0.001	288
	Development of digestive organ tumor	0.001	215
	Gastro-esophageal carcinoma	0.001	143
	Gastroesophageal cancer	0.001	146
	Gastric cancer	0.001	139
	Colon cancer	0.001	175
	Colorectal adenocarcinoma	0.001	173
	Gastric carcinoma	0.001	135

	Upper gastrointestinal tract tumor	0.001	166
	Non-colon gastrointestinal cancer	0.001	172
	Gastrointestinal tract cancer	0.002	291
	Colon adenocarcinoma	0.002	166
	Colorectal carcinoma	0.002	174
	Upper gastrointestinal carcinoma	0.002	161
	Upper gastrointestinal tract cancer	0.002	164
	Colon carcinoma	0.003	167
	Colorectal tumor	0.005	187
	Colorectal cancer	0.008	184
	Pancreatobiliary tumor	0.020	113
	Digestive system cancer	0.021	302
	Mismatch repair deficient colorectal adenocarcinoma	0.035	4
	Metastatic BRAF V600E mutation positive colon cancer	0.035	3
	Metastatic BRAF V600E mutation positive rectal cancer	0.035	3
	Advanced BRAF V600E mutation positive colon cancer	0.035	3
	Advanced BRAF V600E mutation positive rectal cancer	0.035	3
	Replication error repair positive colorectal tumor	0.037	4
Cancer,Gastrointestinal Disease,Organismal Injury and Abnormalities,Tumor Morphology	Metastatic progressive colorectal cancer	0.020	4
Cancer,Hematological Disease,Immunological Disease,Organismal Injury and Abnormalities	Precursor B-cell acute lymphoblastic leukemia	0.019	31
	Acute lymphoblastic leukemia	0.020	36
	B-cell leukemia	0.036	35
Cancer,Neurological Disease,Organismal Injury and Abnormalities	Central nervous system cancer	0.001	228
	Nervous system neoplasm	0.001	232
	Central nervous system solid tumor	0.001	230
	Brain glioma	0.001	221

	Glioma cancer	0.001	223
	Brain tumor	0.001	222
	Glioma	0.001	225
	Brain cancer	0.001	107
	Gliomatosis cerebri	0.005	99
	Brain astrocytoma	0.014	167
	High grade astrocytoma	0.015	172
	Grade 1-4 astrocytoma	0.016	167
	Grade 3-4 glioma	0.017	185
	Grade 3-4 glioma cancer	0.020	184
	Grade 4 high grade glioma	0.020	165
	Grade 4 malignant glioma	0.020	165
	Grade 4 astrocytoma	0.020	165
	Tumorigenesis of glioblastoma	0.022	2
	Meningioma	0.023	17
Cancer,Organismal Injury and Abnormalities	Breast or colorectal cancer	0.001	220
	Melanoma	0.003	264
	Malignant connective or soft tissue neoplasm	0.007	252
	Abdominal adenocarcinoma	0.007	304
	Formation of solid tumor	0.007	302
	Connective or soft tissue tumor	0.011	253
	Malignant soft tissue neoplasm	0.011	249
	Development of carcinoma	0.012	266
	Cancer of head	0.013	124
	Tumorigenesis of epithelial neoplasm	0.013	267
	Frequency of tumor	0.013	268
	Breast or pancreatic cancer	0.015	170
	Head and neck tumor	0.017	306
	Adenocarcinoma	0.017	306
	Non-hematological solid tumor	0.017	336
	Incidence of tumor	0.019	271
	Head and neck squamous cell carcinoma	0.020	99

	Malignant solid organ tumor	0.021	247
	Nonhematologic malignant neoplasm	0.029	335
	Head and neck cancer	0.032	289
	Extraadrenal retroperitoneal tumor	0.035	123
	Head and neck carcinoma	0.037	280
	Malignant neoplasm of retroperitoneum	0.045	113
Cancer,Organismal Injury and Abnormalities,Reproductive System Disease	Breast or ovarian carcinoma	0.028	117
	Breast carcinoma	0.034	84
	Breast cancer	0.044	99
	Mammary tumor	0.049	100
Cancer,Organismal Injury and Abnormalities,Respiratory Disease	Stage IIIB primary non-squamous non-small cell lung carcinoma	0.044	2
	Stage IV primary non-squamous non-small cell lung carcinoma	0.044	2
	Primary EGFR mutation positive non-small cell lung carcinoma	0.044	2
	Stage IV EGFR activating mutation positive EGFR T790M mutation negative nonsquamous non-small cell lung carcinoma	0.044	2
	EGFR T790M mutation negative EGFR exon 20 insertion mutation negative non-small cell lung carcinoma	0.044	2
Cancer,Organismal Injury and Abnormalities,Tumor Morphology	Regression of tumor	0.035	3
Cardiovascular Disease,Cardiovascular System Development and Function,Organ Morphology,Organismal Development,Organismal Injury and Abnormalities,Skeletal and Muscular Disorders	Dilated cardiomyopathy	0.042	13
Cardiovascular System Development and Function,Cellular Development,Cellular Growth and Proliferation	Colony formation of endothelial cell lines	0.044	2
Cardiovascular System Development and Function,Organ Development,Organ Morphology	Contraction of heart	0.020	7
Cell Cycle	Arrest in interphase of tumor cell lines	0.017	19
	Arrest in interphase	0.038	20
	Arrest in G1 phase of tumor cell lines	0.043	13



Cell-To-Cell Signaling and Interaction	Activation of cells	0.007	25
Cell-To-Cell Signaling and Interaction,Hematological System Development and Function	Activation of blood cells	0.020	19
Cellular Development	Epithelial-mesenchymal transition of tumor cell lines	0.045	10
Cellular Development,Cellular Growth and Proliferation,Hematological System Development and Function,Hematopoiesis,Tissue Development	Development of hematopoietic progenitor cells	0.017	11
Cellular Movement	Cell movement of tumor cell lines	0.026	46
	Migration of tumor cell lines	0.029	41
	Migration of cells	0.042	57
	Homing of tumor cell lines	0.049	9
Cellular Movement,Nervous System Development and Function	Migration of neuroglia	0.017	3
Connective Tissue Disorders,Inflammatory Disease,Inflammatory Response,Organismal Injury and Abnormalities,Skeletal and Muscular Disorders	Inflammation of joint	0.044	39
Dermatological Diseases and Conditions,Organismal Injury and Abnormalities	Skin lesion	0.034	244
Developmental Disorder,Hereditary Disorder,Neurological Disease,Organismal Injury and Abnormalities	CHARGE syndrome	0.029	3
Gene Expression	Activation of DNA endogenous promoter	0.001	41
	Transcription	0.002	66
	Transcription of RNA	0.003	59
	Transcription of DNA	0.007	48
	Expression of RNA	0.014	65
	Synthesis of rRNA	0.035	3
Hematological System Development and Function,Hematopoiesis	Development of hematopoietic system	0.013	12
Neurological Disease,Organismal Injury and Abnormalities	Cerebral disorder	0.011	106

Supplemental Table S4. Associations between Proxies of Cumulative Fireground Exposures and DNA Methylation (q&lt;0.05)

Genomic Location <sup>a</sup>	Gene Name	Fire-Hours, All Fires		Fire-Runs, All Fires		Fire-Hours, Structure Fires		Fire-Runs, Structure Fires	
		Estimate (SE) <sup>b</sup>	q-value	Estimate (SE) <sup>b</sup>	q-value	Estimate (SE) <sup>b</sup>	q-value	Estimate (SE) <sup>b</sup>	q-value
chr1:1293868	<i>MXRA8</i>	-0.0139 (0.0066)	0.14	-0.0164 (0.0057)	0.04	-0.0097 (0.0072)	0.37	-0.0134 (0.0077)	0.19
chr1:1912135	<i>CFAP74</i>	0.0174 (0.0056)	0.05	0.016 (0.0049)	0.02	0.0164 (0.0063)	0.12	0.0171 (0.0068)	0.08
chr1:2027575	<i>PRKCZ</i>	0.0144 (0.0052)	0.07	0.0152 (0.0045)	0.02	0.0111 (0.0058)	0.23	0.0168 (0.0061)	0.06
chr1:8797440	<i>RERE</i>	-0.0312 (0.0107)	0.07	-0.0291 (0.0095)	0.04	-0.0315 (0.0117)	0.11	-0.0357 (0.0125)	0.05
chr1:11795976	<i>AGTRAP</i>	-0.0234 (0.0084)	0.07	-0.0209 (0.0074)	0.04	-0.019 (0.0093)	0.22	-0.0239 (0.0099)	0.09
chr1:27874526	<i>AHDC1</i>	0.0152 (0.0063)	0.11	0.0154 (0.0054)	0.04	0.011 (0.007)	0.31	0.0147 (0.0074)	0.14
chr1:32670695	<i>IQCC</i>	0.0334 (0.007)	0.01	0.0322 (0.0061)	0.00	0.0335 (0.0078)	0.04	0.0397 (0.0083)	0.00
chr1:45254092	<i>BEST4</i>	-0.0268 (0.0088)	0.06	-0.0277 (0.0076)	0.02	-0.0218 (0.01)	0.19	-0.0234 (0.0108)	0.12
chr1:97303097	NA	0.0054 (0.0021)	0.10	0.0055 (0.0018)	0.04	0.0036 (0.0024)	0.31	0.0053 (0.0025)	0.13
chr1:109843435	<i>MYBPHL</i>	-0.0245 (0.0078)	0.05	-0.0252 (0.0068)	0.02	-0.0256 (0.0086)	0.09	-0.0374 (0.0089)	0.01
chr1:150668227	<i>GOLPH3L</i>	-0.0257 (0.0097)	0.09	-0.0254 (0.0085)	0.04	-0.0262 (0.0107)	0.14	-0.0323 (0.0113)	0.05
chr1:156865043	<i>PEAR1</i>	-0.0126 (0.0079)	0.23	-0.01 (0.0071)	0.24	-0.02 (0.0084)	0.15	-0.0264 (0.009)	0.05
chr1:185227307	<i>SWT1</i>	0.0135 (0.006)	0.13	0.0144 (0.0052)	0.05	0.0091 (0.0067)	0.36	0.012 (0.0071)	0.20
chr1:192736213	NA	-0.0096 (0.004)	0.11	-0.0102 (0.0034)	0.04	-0.0086 (0.0044)	0.22	-0.0106 (0.0047)	0.11
chr1:204542634	NA	0.0213 (0.007)	0.05	0.021 (0.006)	0.02	0.0154 (0.0079)	0.22	0.0156 (0.0085)	0.17
chr1:206971195	<i>IL19</i>	-0.021 (0.0097)	0.13	-0.0249 (0.0084)	0.04	-0.0156 (0.0108)	0.34	-0.0263 (0.0114)	0.10
chr1:228112951	<i>WNT9A</i>	0.0202 (0.0081)	0.10	0.0248 (0.0068)	0.02	0.0102 (0.0091)	0.44	0.0187 (0.0096)	0.15
chr1:235931377	<i>LYST</i>	-0.0429 (0.0119)	0.04	-0.0414 (0.0103)	0.01	-0.0406 (0.0133)	0.09	-0.0492 (0.014)	0.03
chr2:54756403	<i>RPL23AP32</i>	0.009 (0.0027)	0.05	0.0091 (0.0024)	0.02	0.0057 (0.0031)	0.25	0.0053 (0.0034)	0.24
chr2:70792316	NA	0.0094 (0.0042)	0.13	0.0102 (0.0037)	0.04	0.0051 (0.0048)	0.45	0.01 (0.005)	0.14
chr2:109941286	<i>SH3RF3</i>	0.0048 (0.0023)	0.14	0.0036 (0.002)	0.16	0.007 (0.0024)	0.10	0.0082 (0.0026)	0.04
chr2:114034595	<i>PAX8</i>	-0.0234 (0.0076)	0.05	-0.0213 (0.0067)	0.03	-0.0178 (0.0084)	0.20	-0.0187 (0.0092)	0.13

chr2:178109973	<i>NFE2L2</i>	-0.0242 (0.0126)	0.17	-0.0323 (0.0109)	0.04	-0.0121 (0.0139)	0.55	-0.0248 (0.0149)	0.20
chr2:201593511	<i>AOX2P</i>	-0.0196 (0.0066)	0.06	-0.0174 (0.0058)	0.04	-0.0146 (0.0075)	0.23	-0.0177 (0.0081)	0.12
chr2:240044446	<i>HDAC4</i>	0.0149 (0.006)	0.10	0.0139 (0.0052)	0.05	0.0181 (0.0065)	0.10	0.0201 (0.007)	0.05
chr2:241990667	<i>SNED1</i>	0.0174 (0.0055)	0.05	0.0177 (0.0047)	0.02	0.0142 (0.0062)	0.17	0.0166 (0.0066)	0.08
chr3:9811912	<i>CAMK1</i>	-0.0215 (0.0071)	0.06	-0.0173 (0.0065)	0.06	-0.0259 (0.0075)	0.07	-0.027 (0.0081)	0.04
chr3:31145476	NA	-0.0087 (0.0046)	0.17	-0.0068 (0.0041)	0.19	-0.0136 (0.0049)	0.10	-0.0156 (0.0053)	0.05
chr3:46009762	<i>FYCO1</i>	0.0143 (0.0046)	0.05	0.0134 (0.004)	0.02	0.0151 (0.0051)	0.09	0.0178 (0.0054)	0.04
chr3:49966773	<i>MON1A</i>	0.006 (0.0023)	0.10	0.0056 (0.002)	0.05	0.0044 (0.0026)	0.27	0.005 (0.0028)	0.18
chr3:52008487	<i>ABHD14B</i>	-0.0111 (0.0078)	0.27	-0.0123 (0.0068)	0.16	-0.0174 (0.0085)	0.21	-0.0265 (0.0089)	0.05
chr3:58367583	<i>PXK</i>	0.0256 (0.0148)	0.20	0.0271 (0.0129)	0.10	0.0378 (0.016)	0.15	0.0509 (0.0168)	0.04
chr3:89097455	NA	-0.0215 (0.0073)	0.06	-0.0189 (0.0064)	0.04	-0.0223 (0.008)	0.10	-0.0284 (0.0085)	0.04
chr3:109746788	NA	-0.026 (0.0098)	0.09	-0.0228 (0.0087)	0.06	-0.0302 (0.0106)	0.10	-0.0373 (0.0114)	0.04
chr3:132450221	<i>NPHP3-AS1</i>	-0.0278 (0.0125)	0.13	-0.0275 (0.011)	0.07	-0.0294 (0.0137)	0.20	-0.0415 (0.0143)	0.05
chr4:65749341	NA	-0.0556 (0.016)	0.04	-0.0498 (0.0141)	0.02	-0.0634 (0.0175)	0.07	-0.0582 (0.0192)	0.04
chr4:72897317	<i>NPFFR2</i>	0.0168 (0.0052)	0.05	0.0174 (0.0044)	0.01	0.0142 (0.0058)	0.14	0.0186 (0.0062)	0.04
chr4:73969865	<i>ANKRD17</i>	0.0116 (0.0039)	0.06	0.0098 (0.0035)	0.04	0.0105 (0.0044)	0.15	0.0099 (0.0047)	0.13
chr4:76440740	<i>RCHY1</i>	-0.0381 (0.0158)	0.12	-0.0386 (0.0139)	0.05	-0.0447 (0.0172)	0.12	-0.056 (0.0183)	0.04
chr4:111533823	NA	-0.0214 (0.0079)	0.08	-0.0199 (0.0071)	0.04	-0.0195 (0.0087)	0.18	-0.0242 (0.0093)	0.08
chr5:2758088	NA	-0.0138 (0.0073)	0.17	-0.0153 (0.0063)	0.07	-0.0142 (0.008)	0.25	-0.0243 (0.0084)	0.05
chr5:38427885	<i>EGFLAM</i>	-0.0361 (0.0129)	0.07	-0.0333 (0.0114)	0.04	-0.047 (0.0136)	0.07	-0.0602 (0.014)	0.01
chr5:60622671	NA	0.0245 (0.0076)	0.05	0.0261 (0.0066)	0.01	0.0151 (0.0087)	0.26	0.0192 (0.0093)	0.13
chr5:71764958	<i>ZNF366</i>	-0.0366 (0.0103)	0.04	-0.0364 (0.009)	0.01	-0.035 (0.0115)	0.09	-0.0472 (0.0121)	0.02
chr5:88875631	NA	-0.0337 (0.0095)	0.04	-0.0306 (0.0083)	0.02	-0.0325 (0.0106)	0.09	-0.0392 (0.0113)	0.03
chr5:117897957	<i>HRAT56</i>	0.0122 (0.0033)	0.04	0.013 (0.0028)	0.00	0.0059 (0.0039)	0.31	0.0096 (0.0041)	0.10
chr5:142422241	<i>ARHGAP26</i>	0.0075 (0.003)	0.10	0.0085 (0.0025)	0.02	0.0024 (0.0034)	0.61	0.0044 (0.0036)	0.34
chr5:153211415	NA	-0.0231 (0.0099)	0.12	-0.0247 (0.0086)	0.04	-0.0249 (0.0108)	0.17	-0.0354 (0.0115)	0.04
chr5:179709813	<i>MAPK9</i>	0.0073 (0.004)	0.18	0.0075 (0.0035)	0.10	0.0088 (0.0044)	0.22	0.0131 (0.0046)	0.05
chr6:13007033	<i>PHACTR1</i>	-0.0212 (0.0124)	0.21	-0.0186 (0.0109)	0.17	-0.0284 (0.0135)	0.20	-0.0417 (0.0141)	0.05

chr6:13053520	<i>PHACTR1</i>	-0.0419 (0.0126)	0.05	-0.0412 (0.011)	0.02	-0.0379 (0.0141)	0.11	-0.0482 (0.0149)	0.04
chr6:30159309	<i>TRIM26</i>	0.0075 (0.0032)	0.12	0.0095 (0.0027)	0.02	0.0015 (0.0036)	0.77	0.0052 (0.0038)	0.29
chr6:46380623	<i>RCAN2</i>	-0.0267 (0.0104)	0.10	-0.0266 (0.0092)	0.04	-0.0178 (0.0115)	0.31	-0.0225 (0.0124)	0.17
chr6:101880078	<i>GRIK2</i>	-0.0326 (0.0129)	0.10	-0.0346 (0.0112)	0.04	-0.0308 (0.0143)	0.19	-0.0425 (0.0151)	0.05
chr6:152232729	<i>ESR1</i>	-0.0234 (0.0071)	0.05	-0.0198 (0.0064)	0.04	-0.027 (0.0077)	0.07	-0.0318 (0.0082)	0.02
chr7:2158623	<i>MAD1L1</i>	0.0255 (0.0069)	0.04	0.0272 (0.0059)	0.00	0.0178 (0.008)	0.18	0.0235 (0.0084)	0.06
chr7:2663085	NA	-0.0112 (0.0075)	0.26	-0.0087 (0.0066)	0.27	-0.0219 (0.0079)	0.10	-0.0249 (0.0085)	0.05
chr7:14899040	NA	-0.0306 (0.0145)	0.14	-0.0356 (0.0125)	0.04	-0.0203 (0.0163)	0.40	-0.0375 (0.0171)	0.12
chr7:48127925	<i>UPP1</i>	-0.0155 (0.0075)	0.14	-0.0177 (0.0065)	0.05	-0.0134 (0.0083)	0.29	-0.0166 (0.0089)	0.16
chr7:100282651	<i>GIGYF1</i>	0.0157 (0.0047)	0.05	0.0136 (0.0041)	0.02	0.0149 (0.0052)	0.10	0.0166 (0.0056)	0.04
chr7:150086034	<i>ZNF775</i>	-0.0296 (0.0114)	0.09	-0.0291 (0.01)	0.04	-0.024 (0.0128)	0.24	-0.0343 (0.0135)	0.08
chr8:27114746	<i>STMN4</i>	-0.035 (0.009)	0.04	-0.0327 (0.008)	0.01	-0.032 (0.01)	0.09	-0.0369 (0.011)	0.04
chr8:128512692	NA	0.0067 (0.0032)	0.14	0.008 (0.0028)	0.04	0.002 (0.0036)	0.71	0.0056 (0.0039)	0.26
chr9:5186210	<i>INSL6</i>	0.0093 (0.0037)	0.10	0.0092 (0.0032)	0.04	0.0069 (0.0041)	0.27	0.0079 (0.0044)	0.18
chr9:135852984	<i>GFI1B</i>	-0.0263 (0.0098)	0.08	-0.0245 (0.0086)	0.04	-0.0262 (0.0107)	0.14	-0.0308 (0.0114)	0.07
chr9:140174741	<i>C9orf167</i>	0.023 (0.0072)	0.05	0.0217 (0.0063)	0.02	0.0231 (0.008)	0.10	0.0308 (0.0084)	0.02
chr9:140376822	<i>PNPLA7</i>	-0.02 (0.0072)	0.08	-0.021 (0.0063)	0.02	-0.0167 (0.008)	0.20	-0.0264 (0.0084)	0.04
chr10:14338581	<i>FRMD4A</i>	0.0045 (0.0018)	0.11	0.0044 (0.0016)	0.05	0.0038 (0.0021)	0.25	0.0046 (0.0022)	0.13
chr10:76661092	<i>KAT6B</i>	-0.0353 (0.0094)	0.04	-0.0327 (0.0083)	0.01	-0.0348 (0.0105)	0.07	-0.0378 (0.0113)	0.04
chr10:134211857	<i>PWWP2B</i>	-0.0283 (0.0105)	0.08	-0.0279 (0.0092)	0.04	-0.0182 (0.0118)	0.31	-0.0253 (0.0128)	0.14
chr11:1536810	<i>HCCA2</i>	-0.0178 (0.0112)	0.23	-0.0179 (0.0099)	0.15	-0.0277 (0.012)	0.17	-0.0363 (0.0127)	0.05
chr11:5538958	<i>UBQLNL</i>	-0.033 (0.0095)	0.04	-0.0257 (0.0085)	0.04	-0.0368 (0.0104)	0.07	-0.0348 (0.0114)	0.04
chr11:11866554	<i>USP47</i>	-0.0225 (0.0083)	0.08	-0.0153 (0.0075)	0.11	-0.0345 (0.0087)	0.06	-0.0327 (0.0096)	0.04
chr11:47959926	NA	-0.031 (0.0099)	0.05	-0.0283 (0.0086)	0.02	-0.0285 (0.011)	0.12	-0.0357 (0.0117)	0.04
chr11:62600230	<i>STX5</i>	-0.0249 (0.0089)	0.07	-0.0213 (0.0079)	0.05	-0.0285 (0.0096)	0.10	-0.0349 (0.0102)	0.04
chr11:65378788	<i>MAP3K11</i>	-0.0115 (0.0063)	0.18	-0.011 (0.0055)	0.12	-0.0187 (0.0067)	0.10	-0.0216 (0.0071)	0.04
chr11:68795647	NA	-0.0251 (0.0069)	0.04	-0.0186 (0.0062)	0.04	-0.0253 (0.0076)	0.07	-0.0254 (0.0082)	0.04
chr11:79613887	NA	-0.0266 (0.0096)	0.07	-0.0281 (0.0083)	0.02	-0.027 (0.0106)	0.13	-0.0335 (0.0113)	0.05

chr11:119537405	<i>PVRL1</i>	-0.0185 (0.0082)	0.13	-0.0151 (0.0072)	0.11	-0.0228 (0.0089)	0.13	-0.0288 (0.0094)	0.04
chr12:11081043	<i>PRH2</i>	0.006 (0.0026)	0.13	0.0069 (0.0023) -0.0138 (0.0044)	0.04	0.0057 (0.0029)	0.23	0.0082 (0.0031)	0.07
chr12:42102842	NA	-0.0144 (0.0051)	0.07	-0.0188 (0.0062)	0.03	-0.0141 (0.0056)	0.13	-0.0166 (0.006)	0.06
chr12:52435577	<i>NR4A1</i>	-0.0169 (0.0071)	0.12	-0.0229 (0.0067)	0.04	-0.0184 (0.0077)	0.15	-0.028 (0.0079)	0.03
chr12:54402050	<i>HOXC8</i>	-0.0241 (0.0077)	0.05	-0.0368 (0.012) -0.0159 (0.0056)	0.02	-0.0238 (0.0084)	0.10	-0.0302 (0.009)	0.04
chr12:119621039	<i>HSPB8</i>	-0.0352 (0.0138)	0.10	-0.0159 (0.0047)	0.04	-0.0212 (0.0153)	0.36	-0.0328 (0.0164)	0.14
chr12:120559003	NA	-0.0153 (0.0064)	0.12	-0.0254 (0.0086)	0.04	-0.0141 (0.007)	0.22	-0.02 (0.0075)	0.07
chr12:120802252	<i>MS1</i>	0.0141 (0.0054)	0.09	-0.0137 (0.0067)	0.04	0.0117 (0.0061)	0.23	0.0149 (0.0065)	0.10
chr13:35043968	<i>LINC00457</i>	-0.022 (0.01)	0.13	-0.0494 (0.0147)	0.04	-0.0273 (0.0108)	0.13	-0.047 (0.0109)	0.01
chr13:72778607	NA	-0.0168 (0.0075)	0.13	-0.0563 (0.015) -0.0227 (0.0079)	0.11	-0.0221 (0.0081)	0.10	-0.0247 (0.0087)	0.05
chr14:24858912	NA	-0.0461 (0.0169)	0.08	-0.0157 (0.0058)	0.02	-0.0365 (0.0191)	0.23	-0.0498 (0.0206)	0.09
chr14:63785523	<i>GPHB5</i>	-0.0599 (0.0168)	0.04	-0.0227 (0.0079)	0.02	-0.0665 (0.0176)	0.07	-0.0762 (0.0191)	0.02
chr14:105955879	<i>C14orf80</i>	-0.0205 (0.009)	0.13	-0.0157 (0.0058)	0.04	-0.0179 (0.01)	0.25	-0.0228 (0.0108)	0.13
chr15:45406362	<i>DUOX2</i>	-0.015 (0.0066)	0.13	0.01 (0.0029)	0.05	-0.0134 (0.0073)	0.25	-0.0221 (0.0077)	0.05
chr15:58011290	NA	0.0101 (0.0034)	0.06	0.0102 (0.0042) -0.0195 (0.0068)	0.02	0.0079 (0.0038)	0.20	0.0101 (0.004)	0.08
chr15:68933603	<i>CORO2B</i>	0.0118 (0.0048)	0.11	0.0151 (0.0057) 0.0116 (0.004) -0.0177 (0.0077)	0.08	0.0162 (0.0051)	0.09	0.0173 (0.0055)	0.04
chr16:1386290	<i>BAIAP3</i>	-0.0189 (0.0077)	0.11	0.0136 (0.0047)	0.04	-0.0233 (0.0082)	0.10	-0.0323 (0.0086)	0.02
chr16:1420171	<i>UNKL</i>	0.0137 (0.0054)	0.10	0.0151 (0.0057)	0.04	0.0102 (0.0061)	0.27	0.0117 (0.0065)	0.17
chr16:2086421	<i>SLC9A3R2</i>	0.0159 (0.0064)	0.10	0.0116 (0.004) -0.0177 (0.0077)	0.05	0.0183 (0.007)	0.12	0.0248 (0.0074)	0.04
chr16:28922391	<i>RABEP2</i>	0.0093 (0.0046)	0.16	0.0116 (0.004) -0.0177 (0.0077)	0.04	0.0028 (0.0052)	0.71	0.0095 (0.0055)	0.18
chr16:57984539	<i>CNGB1</i>	-0.0201 (0.0087)	0.13	0.0221 (0.0064)	0.08	-0.0253 (0.0093)	0.11	-0.033 (0.0098)	0.04
chr16:88096588	<i>BANP</i>	0.0194 (0.0075)	0.09	0.0118 (0.0049)	0.02	0.0089 (0.0085)	0.46	0.0157 (0.009)	0.18
chr16:88979098	<i>CBFA2T3</i>	0.0108 (0.0057)	0.17	0.0118 (0.0049)	0.08	0.0113 (0.0063)	0.25	0.0201 (0.0065)	0.04
chr16:89922539	<i>SPIRE2</i>	0.0186 (0.006)	0.05	0.015 (0.0053)	0.04	0.0202 (0.0065)	0.09	0.0188 (0.0071)	0.07
chr17:1059336	<i>ABR</i>	0.0103 (0.0051)	0.15	0.0099 (0.0044)	0.09	0.015 (0.0054)	0.10	0.0187 (0.0058)	0.04
chr17:2861947	<i>RAP1GAP2</i>	0.0169 (0.0052)	0.05	0.0143 (0.0047)	0.04	0.0178 (0.0057)	0.09	0.0179 (0.0063)	0.05
chr17:4350829	<i>SPNS3</i>	0.0081 (0.0035)	0.13	0.0087 (0.0031)	0.04	0.005 (0.004)	0.39	0.0086 (0.0042)	0.13
chr17:4917032	<i>KIF1C</i>	0.0115 (0.004)	0.07	0.0106 (0.0035) -0.0127 (0.0063)	0.04	0.0121 (0.0044)	0.10	0.0165 (0.0046)	0.02
chr17:7083015	<i>ASGR1</i>	-0.0163 (0.0071)	0.13	-0.0127 (0.0063)	0.12	-0.0243 (0.0076)	0.09	-0.0257 (0.0082)	0.04

chr17:10541620	<i>MYH3</i>	-0.0022 (0.0007)	0.05	-0.0022 (0.0006)	0.02	-0.0023 (0.0008)	0.09	-0.003 (0.0008)	0.02
chr17:19628421	NA	-0.031 (0.0086)	0.04	-0.0281 (0.0077)	0.02	-0.035 (0.0091)	0.07	-0.0374 (0.0098)	0.02
chr17:27441752	<i>MYO18A</i>	0.0183 (0.0061)	0.06	0.0186 (0.0054)	0.02	0.0152 (0.0068)	0.18	0.0153 (0.0073)	0.13
chr17:39554246	<i>KRT31</i>	-0.0156 (0.0055)	0.07	-0.0163 (0.0047)	0.02	-0.0112 (0.0062)	0.25	-0.015 (0.0066)	0.11
chr17:76850256	<i>TIMP2</i>	-0.0343 (0.0092)	0.04	-0.0324 (0.0079)	0.01	-0.0256 (0.0104)	0.14	-0.0286 (0.0111)	0.08
chr18:9643805	NA	-0.0473 (0.0143)	0.05	-0.043 (0.0126)	0.02	-0.0476 (0.0159)	0.09	-0.0541 (0.0171)	0.04
chr18:47813745	<i>CXXC1</i>	-0.0082 (0.0028)	0.07	-0.0075 (0.0025)	0.04	-0.0068 (0.0032)	0.20	-0.0077 (0.0034)	0.11
chr18:55906325	<i>NEDD4L</i>	-0.0313 (0.0112)	0.07	-0.029 (0.0097)	0.04	-0.0343 (0.0122)	0.10	-0.0396 (0.013)	0.04
chr19:1612208	<i>TCF3</i>	0.0141 (0.0062)	0.13	0.0151 (0.0054)	0.05	0.0131 (0.0068)	0.23	0.0182 (0.0073)	0.08
chr19:2062522	NA	0.0201 (0.0069)	0.07	0.0183 (0.0061)	0.04	0.0238 (0.0076)	0.09	0.0271 (0.0081)	0.04
chr19:2065374	NA	0.0177 (0.0068)	0.09	0.0191 (0.0059)	0.02	0.0178 (0.0074)	0.15	0.0251 (0.0079)	0.04
chr19:2579745	<i>GNG7</i>	-0.0223 (0.0072)	0.05	-0.0203 (0.0064)	0.03	-0.0201 (0.008)	0.13	-0.0218 (0.0087)	0.08
chr19:2706834	NA	-0.0176 (0.0083)	0.14	-0.0187 (0.0073)	0.06	-0.019 (0.0091)	0.20	-0.0285 (0.0095)	0.05
chr19:4278055	<i>SHD</i>	-0.0217 (0.0077)	0.07	-0.022 (0.0066)	0.02	-0.02 (0.0084)	0.15	-0.0257 (0.009)	0.05
chr19:4540065	<i>LRG1</i>	-0.0242 (0.0089)	0.08	-0.021 (0.0079)	0.06	-0.0327 (0.0096)	0.07	-0.0383 (0.0103)	0.02
chr19:17448937	<i>GTPBP3</i>	0.0009 (0.0004)	0.12	0.0009 (0.0003)	0.04	0.0007 (0.0004)	0.28	0.0011 (0.0004)	0.08
chr19:17597999	<i>SLC27A1</i>	0.0105 (0.0049)	0.14	0.0106 (0.0043)	0.07	0.0102 (0.0055)	0.24	0.0165 (0.0057)	0.05
chr19:17631991	<i>PGLS</i>	0.0217 (0.0076)	0.07	0.0243 (0.0065)	0.02	0.0167 (0.0085)	0.22	0.028 (0.0089)	0.04
chr19:19426589	<i>SUGP1</i>	0.0204 (0.0063)	0.05	0.0171 (0.0056)	0.04	0.0188 (0.007)	0.11	0.0167 (0.0076)	0.12
chr19:33889481	<i>PEPD</i>	0.0155 (0.0068)	0.13	0.0195 (0.0058)	0.02	0.0111 (0.0075)	0.33	0.0186 (0.0079)	0.10
chr19:35502231	<i>GRAMD1A</i>	-0.0162 (0.008)	0.16	-0.0192 (0.0069)	0.05	-0.0143 (0.0089)	0.29	-0.0268 (0.0092)	0.05
chr19:40709597	<i>MAP3K10</i>	0.0137 (0.0044)	0.05	0.0117 (0.0039)	0.04	0.0143 (0.0049)	0.10	0.0162 (0.0052)	0.04
chr19:40883570	<i>PLD3</i>	0.0116 (0.0047)	0.11	0.0116 (0.0041)	0.04	0.0111 (0.0052)	0.20	0.016 (0.0055)	0.05
chr19:42557118	<i>GRIK5</i>	0.0147 (0.0055)	0.08	0.0137 (0.0048)	0.04	0.0094 (0.0062)	0.31	0.009 (0.0066)	0.29
chr19:42582914	<i>ZNF574</i>	0.0175 (0.0063)	0.07	0.0173 (0.0055)	0.03	0.018 (0.007)	0.12	0.0228 (0.0073)	0.04
chr20:33543028	<i>GSS</i>	-0.0169 (0.0068)	0.10	-0.015 (0.006)	0.07	-0.0204 (0.0073)	0.10	-0.0223 (0.0078)	0.05
chr20:56419097	NA	0.0092 (0.0045)	0.15	0.0084 (0.004)	0.10	0.0122 (0.0049)	0.14	0.0149 (0.0052)	0.05
chr21:44462317	NA	0.0221 (0.0067)	0.05	0.0192 (0.0059)	0.02	0.0201 (0.0074)	0.11	0.0227 (0.008)	0.05
chr21:44914774	NA	-0.0231 (0.0087)	0.09	-0.0233 (0.0076)	0.04	-0.0272 (0.0096)	0.10	-0.0334 (0.0103)	0.04
chr22:38137445	<i>TRIOBP</i>	-0.0141 (0.0065)	0.13	-0.0154 (0.0056)	0.05	-0.0109 (0.0072)	0.31	-0.0185 (0.0076)	0.09

chr22:39348639	NA	-0.0265 (0.0078)	0.05	-0.0234 (0.0069)	0.02	-0.0288 (0.0086)	0.07	-0.0355 (0.009)	0.02
chrX:48620142	<i>GLOD5</i>	0.0141 (0.0059)	0.12	0.0122 (0.0052)	0.08	0.0164 (0.0065)	0.13	0.0199 (0.0069)	0.05
chrX:68759322	NA	0.0146 (0.0077)	0.17	0.0189 (0.0066)	0.04	-0.0013 (0.0086)	0.92	0.0074 (0.0093)	0.54

<sup>a</sup> Genomic location is according to genome build GRCh37/hg19

<sup>b</sup> Effect estimates represent the change in proportion of DNA methylation at the locus for each ln-transformed unit of the fire-variable in linear mixed effects models adjusted for batch, cell type estimates, Hispanic ethnicity, estimated smoking pack-years, time between baseline and follow-up, and a random intercept for individual. Separate models were run for each fire-variable.

NA means the CpG site is not within a gene or within a known feature (e.g. promoter) of a specific gene.

Statistically significant at q-value<0.05

## SUPPLEMENTAL METHODS

Samples were randomized and hybridized to chips across three batches (one at the University of Utah DNA Sequencing and Genomics Core Facility, and two batches at the University of Michigan Advanced Genomics Core), scanned by experienced personnel, and processed as we previously described.[1] Briefly, raw image files were read with the R package minfi, and the ENmix package was used for quality control and normalization.[2] Probes were removed if at least 5% of samples were not detected ( $p$ -value $>1e^{-16}$  compared to background). Background correction was performed with noob and dye bias correction with Regression on Logarithm of Internal Control probes followed by quantile normalization.[3] Cross-reactive probes and probes with SNPs in the CpG or single-base extension site were excluded. Five pairs that failed quality control for at least one sample were excluded. The final dataset consisted of 759,346 CpG sites and 100 samples (50 pairs).

The proportion of six blood cell types were estimated using reference data from sorted blood leukocytes according to the algorithm established by Houseman *et al.*[4] We used data from control probes included on each chip for surrogate variable analysis, and created three principal components (PCs) explaining 92% of the technical variance in the data; these are used as covariates in downstream models to adjust for batch effects.[5] While all participants were reported to be current non-smokers, past exposure was uncertain. We used an algorithm based on the DNA methylation data to estimate lifetime smoking pack-years.[6] Since this estimation is highly correlated with age, we regressed pack-years on age and adjusted for the residuals in statistical models (referred to as “pack-years residual”).

### References:

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