## ORCA - Online Research @ Cardiff

## PRIFYSGOL CAERDYB

This is an Open Access document downloaded from ORCA, Cardiff University's institutional repository:https://orca.cardiff.ac.uk/id/eprint/105236/

This is the author's version of a work that was submitted to / accepted for publication.

Citation for final published version:
Lee, Jong-Min, Chao, Michael J., Harold, Denise, Abu Elneel, Kawther, Gillis, Tammy, Holmans, Peter, Jones, Lesley, Orth, Michael, Myers, Richard H., Kwak, Seung, Wheeler, Vanessa C, MacDonald, Marcy E. and Gusella, James F. 2017. A modifier of Huntington's disease onset at the MLH1 locus. Human Molecular Genetics 26 (19), pp. 3859-3867. $10.1093 / \mathrm{hmg} / \mathrm{ddx} 286$

Publishers page: http://dx.doi.org/10.1093/hmg/ddx286
Please note:
Changes made as a result of publishing processes such as copy-editing, formatting and page numbers may not be reflected in this version. For the definitive version of this publication, please refer to the published source. You are advised to consult the publisher's version if you wish to cite this paper.

This version is being made available in accordance with publisher policies. See http://orca.cf.ac.uk/policies.html for usage policies. Copyright and moral rights for publications made available in ORCA are retained by the copyright holders.

## A modifier of Huntington's disease onset at the MLH1 locus

Jong-Min Lee ${ }^{1,2,3, \$}$, Michael J. Chao ${ }^{1,2}$, Denise Harold ${ }^{4, \$, \&}$, Kawther Abu Elneel ${ }^{1}$, Tammy Gillis ${ }^{1}$, Peter Holmans ${ }^{4, \$}$, Lesley Jones ${ }^{4, \$}$, Michael Orth ${ }^{5, \$}$, Richard H. Myers ${ }^{6, \$}$, Seung Kwak ${ }^{7, \$}$, Vanessa
C. Wheeler ${ }^{1,2, \$}$, Marcy E. MacDonald ${ }^{1,2,3, \$}$, and James F. Gusella ${ }^{1,3,8, \$,{ }^{*}}$
${ }^{1}$ Molecular Neurogenetics Unit, Center for Genomic Medicine, Massachusetts General Hospital, Boston, MA 02114, USA
${ }^{2}$ Department of Neurology, Harvard Medical School, Boston, MA 02115, USA
${ }^{3}$ Medical and Population Genetics Program, the Broad Institute of M.I.T. and Harvard, Cambridge, MA 02142, USA
${ }^{4}$ Medical Research Council (MRC) Centre for Neuropsychiatric Genetics and Genomics, Department of Psychological Medicine and Neurology, School of Medicine, Cardiff University, Cardiff, United Kingdom
${ }^{5}$ Department of Neurology, University of Ulm, Germany
${ }^{6}$ Department of Neurology and Genome Science Institute, Boston University School of Medicine, Boston, MA 02118, USA
${ }^{7}$ CHDI Foundation, Princeton, NJ 08540, USA
${ }^{8}$ Department of Genetics, Harvard Medical School, Boston, MA 02115, USA
${ }^{\$}$ Founding GeM-HD Consortium investigators
${ }^{\text {\& }}$ Present address: School of Biotechnology, Dublin City University, Dublin 9, Ireland

* To whom correspondence should be addressed: James F, Gusella (Tel: 717-726-5724; Email, gusella@helix.mgh.harvard.edu), Molecular Neurogenetics Unit, CPZN5.252, 185 Cambridge St., Massachusetts General Hospital, Boston, MA 02114, USA


#### Abstract

Huntington's disease (HD) is a dominantly inherited neurodegenerative disease caused by an expanded CAG repeat in HTT. Many clinical characteristics of HD such as age at motor onset are determined largely by the size of HTTCAG repeat. However, emerging evidence strongly supports a role for other genetic factors in modifying the disease pathogenesis driven by mutant huntingtin. A recent genome-wide association analysis to discover genetic modifiers of HD onset age provided initial evidence for modifier loci on chromosomes 8 and 15 and suggestive evidence for a locus on chromosome 3. Here, genotyping of candidate SNPs in a cohort of 3,314 additional HD subjects yields independent confirmation of the former two loci and moves the third to genome-wide significance at $M L H 1$, a locus whose mouse orthologue modifies CAG length-dependent phenotypes in a Htt-knock-in mouse model of HD. Both quantitative and dichotomous association analyses implicate a functional variant on $\sim 32 \%$ of chromosomes with beneficial modifier effect that delays HD motor onset by 0.7 years/allele. Genomic DNA capture and sequencing of the modifier haplotype localize the functional variation to a 78 kb region spanning the 3'end of MLH 1 and the 5 'end of the neighboring LRRFIP2, and marked by an isoleucine-valine missense variant in MLH1. Analysis of eQTLs provides modest support for altered regulation of MLH1 and LRRFIP2, raising the possibility that the modifier affects regulation of both genes. Finally, polygenic modification score and heritability analyses suggest the existence of additional genetic modifiers, supporting expanded, comprehensive genetic analysis of larger HD datasets.


## Introduction

Huntington's disease (HD) is a dominantly inherited neurodegenerative disorder in which an unstable expanded CAG trinucleotide repeat of $>35$ units in $H T T$, the 4 p16.3 gene encoding huntingtin (1), precipitates a characteristic movement disorder and premature death $(2,3)$. The length of the CAG expansion is the primary determinant of the rate of the HD disease process since its size is inversely correlated with the age at onset of neurologic symptoms (4-8). However, other genetic factors also play a role in influencing the time to onset $(9,10)$. A recent genome-wide association (GWA) analysis of the difference between actual and CAG-predicted age at onset in $\sim 4,000 \mathrm{HD}$ individuals identified genome-wide significant modifier loci, one with two independent modifier signals on chromosome 15 and a single modifier signal on chromosome 8 (11). In addition, a suggestive association signal was detected in chromosome 3p22.2 near mutL homolog 1 (MLH1) (11), known for its involvement in DNA mismatch repair (12). Dominant loss of function mutation of MLH1 are associated with Lynch Syndrome (Hereditary Non-Polyposis Colon Cancer type 2 or HNPCC2; MIM\#609310), in which tumors display instability of dinucleotide repeats. The 3p22 GWA signal in our study contributed to pathway analyses that further highlighted a role for DNA maintenance processes in HD modification, supporting the hypothesis that somatic CAG instability may influence onset age suggested previously by a correlation between high instability of the expanded repeat in HD postmortem brain tissue and an earlier age at motor onset (13). Moreover, genetic ablation of the murine MLH1 homolog, Mlh1, in Htt CAG repeat knock-in mice eliminated instability of the expanded repeat and ameliorated nuclear huntingtin staining, a striatal disease phenotype (14). To obtain independent confirmation of the loci on chromosomes 8 and 15 and to test the significance of several other potential modifier loci, especially that in 3p22.2, we employed the Fluidigm platform to genotype individual
candidate SNPs in a large independent cohort of HD individuals: 3,314 participants from the European Huntington's Disease Network (EHDN) Registry collection.

## Results

## Single SNP association analysis reveals a 3rd genome-wide significant modifier locus

Study subjects analyzed here displayed distributions of age at onset corrected for CAG repeat size (i.e., residual age at onset) and minor allele frequencies (MAF) comparable to the previous GWA samples (Figures S1-S2). A number of the top scoring SNPs from the original GWA study (11, 15) were not suitable for the Fluidigm genotyping platform (https://www.fluidigm.com/), so we substituted other variants that captured the same modifier signals. Ultimately, we genotyped the replication set for rs34852161 at the chromosome 8 locus, rs150393409 and rs35811129 representing independent modifier effects in the same region of chromosome 15, rs116483964 and rs1799977 at the 3p22.2 locus and individual SNPs at 57 additional loci chosen for being amenable to the platform and having a p-value $<0.005$ in either quantitative or dichotomous analysis from the original GWA (11) (Table S1). Quantitative association analysis using residual age at motor onset as the phenotype revealed nominally significant scores for rs34852161 on chromosome 8 and rs150393409 on chromosome 15 , while rs35811129 on chromosome 15 yielded genome-wide significance (p-value 2E-10) in the replication set (Table 1; Table S2). In meta-analysis with the prior GWA study, all three yielded genome-wide significant scores, confirming the modifier effects reported previously (11). At the 3p22.2 locus, both rs1799977 in MLH1 and rs116483964 in the adjacent LRRFIP2 exhibited nominally significant p-values (Table 1). Meta-analysis
combining the replication data and GWA analysis results raised both to genome-wide significance (8.84E-09 and 1.19E-08, respectively) (Table 1; Figure 1A, filled red circles).

As this finding adds an additional locus to the list of genome-wide significant HD modifiers, we also carried out dichotomous analysis to evaluate the possibility that the significant association in quantitative analysis was driven by a few individuals with extreme residuals. Comparison of allele frequencies between the top and bottom $20 \%$ phenotypic extreme samples from the combined data (1,478 samples for each extreme group) also revealed genome-wide significance for rs1799977 (p-value, 5.3E-09) and rs116483964 (p-value, 5.6E-09) (Table 2A). Conditional analysis demonstrated that both SNPs appear to capture a single modifier effect (Table 2B). The minor allele of each SNP was associated with delaying age at onset by approximately 0.7 years, explaining $0.5 \%$ of the residual age at onset in the combined data set. Of the remaining 57 independent loci tested, none attained genome-wide significance in the meta-analysis of GWA and Fluidigm data sets, although 3 were nominally significant (p-value $<0.05$ ) in the latter (Table S2).

## Narrowed localization of the Chr3 functional variation responsible for modification of HD

 The rs 1799977 minor allele is a missense (isoleucine to valine) variant in MLH1, with a reported allele frequency of about $32.5 \%$ in 1,000 Genomes Project Europeans. As noted above, MLH1 is involved in DNA mismatch repair $(12,16)$ and HD CAG repeat instability $(14)$, and inactivating mutations are present in some Lynch Syndrome families (17). SNP rs116483964, with a comparable minor allele frequency, is in an early intron of the immediately adjacent gene, LRRFIP2, whose product, Leucine Rich Repeat (In FLII) Interacting Protein 2, is involved in protein-protein interactions that regulate Wnt-signaling (18). LRRFIP2 is deleted together withMLH1 as a founder mutation in some Portuguese Lynch syndrome families (19). In the original GWA study, there were other SNPs with comparable p-values at this locus that were not amenable to genotyping on the Fluidigm platform. To seek the variation responsible for the modifier effect, we selected 7 unrelated HD subjects homozygous for the minor allele of rs144287831, the top SNP from the GWA analysis (11), and with positive age of onset residuals $>4$, and performed genomic DNA capture and sequencing of the 771 kb region (Figure 1 A , a blue horizontal bar; Chr3:36,832,273-37,603,667) spanning TRANK1, EPM2AIP1, MLH1, LRRFIP2, GOLGA4, C3orf35 and a portion of ITGA9. These 14 chromosomes from 7 HD individuals were near identical for all frequent (> 1\%) reported SNPs across a haplotype of approximately 100 kb between Chr3:37,043,009-37,142,847 (Figure 1A, a red horizontal bar; Table S3). Encompassed by this haplotype were the minor alleles for the 7 top scoring markers from the GWA, all of which have a frequency of 0.31-0.32 in our HD dataset (Table 3). Each of these markers shows a striking shift of the minor allele toward the $4^{\text {th }}$ quartile of the age of onset residual distribution, indicative of a contribution of a chromosome bearing this 7-marker haplotype to later than expected onset (Table 3).

The GWA and capture sequencing data both argue that $0.31-0.32$ is the frequency of the responsible functional modifier variation at this locus in European HD subjects. First, the 100 kb shared haplotype also contains many polymorphic sites of higher MAF ( 107 sites MAF $>0.32$ ) in Europeans, but these all yielded weaker significance scores in both quantitative and dichotomous association analysis (Figure 1B, filled grey circles), indicating that signal from the allele on the modifier haplotype is diluted by the presence of the same allele on many non-modifier chromosomes. Second, all markers with MAF $<0.31$ ( 70 sites with MAF $>0.02$ ) yielded weaker
significance scores in the GWA analysis (Figure 1B, open grey circles), indicating that they did not fully capture the modifier effect and arguing against the effect being contributed by only a subset of the chromosomes marked by the top SNPs. Finally, our capture sequencing of these 14 candidate modifier chromosomes did not identify any shared novel variants that could be responsible for modification (Table S3). Consequently, the modifier effect is likely to be due to one or more of the markers listed in Table 3, acting either individually or together through part or all of the haplotype that they define. Although we cannot completely exclude an undetected structural variation or a change in a simple sequence repeat, as these may remain cryptic to the capture sequencing used, we did exclude the presence of structural variations greater than a few kb using whole genome sequencing of large-insert jumping libraries $(20,21)$. The most attractive candidate variant is rs1799977 since it alters the primary sequence of the MLH1 protein, may impact mildly on its interaction with PMS2 (22) and has been associated with allelic expression of the MLH1 transcript (23). The ancestral A allele of rs1799977 specifies an isoleucine residue at position 219 that is conserved across mammals. The alternate $G$ allele specifies valine, which is present in this conserved region of the MLH1 proteins of some reptiles, birds, fish and lower organisms, consistent with a functional but subtly different MLH1 protein. In candidate studies, this I219V polymorphism has been tested as a low penetrance risk factor or modifier of various cancers, with mixed results, again suggestive of only a subtle functional impact (24-32). Neither rs1799977 nor the other SNPs in the modifier haplotype are listed in the GWAS catalog (2017-0213 release) as associated with genome-wide significance to cancer or other human phenotypes.

## Potential effect of the modifier haplotype on gene expression

The two Chr3 markers used here both yielded significant eQTL signals with expression of multiple genes in the region (MLH1, LRRFIP2, and GOLGA4) in various tissues (GTEx portal, V6; http://www.gtexportal.org/home/). To examine whether the modifier haplotype contributes to any cis-eQTLs, we related the association signals for all GWA SNPs in the Chr3:36,800,00037,800,000 region (Figure 1) to eQTL signals for the local genes. We employed the HaploReg annotation tool (http://archive.broadinstitute.org/mammals/haploreg/haploreg.php) to determine the number of tissues in which the test SNP was significantly associated with expression of the test gene. The results revealed only modest correspondence between GWA modifier association signals and HaploReg eQTL data for MLH1 and a mildly stronger correspondence for LRRFIP2, but no correspondence for other genes in the region (Figure S3). When we directly compared the strength of the GWA modifier association signal for each SNP with that of its eQTL signal in the GTEx database (Figure S4), we found a significant correlation between eQTL signals for LRRFIP2 in putamen and modifier association signals (Figure S4B, top right panel; Pearson's correlation, pvalue $<2.2 \mathrm{E}-16$ ). In an independent data set (BRAINEAC; http://www.braineac.org/), we did not see a significant eQTL association for MLH1 or LRRFIP2, but did observe correlated relationships between exon level QTL signals and modification signals for certain regions of LRRFIP2 (Figure S5). The modifier haplotype was associated with increased levels of LRRFIP2 but not MLH1 mRNA in brain tissues, but this gene-level analysis does not account for different transcript isoforms or address all brain regions (Figure S6; rs1799977). It remains uncertain which particular cell type is responsible for the modifier effect and whether there is a coincident impact on expression of any MLH1 transcript isoform. Notably, one rare transcript isoform of MLH1 is reported to overlap with LRRFIP2, suggesting the possibility that regulatory changes could in
some instances affect expression of both genes. More detailed molecular studies in human HD tissues will be required to determine the precise impact(s) of this modifier haplotype on both MLH1 and LRRFIP2.

## Genetic component of residual age at onset

The four independent genome-wide significant modifier signals at 3 loci explain only a small portion of the variance in residual HD age at onset. Therefore, we evaluated the explanatory power of a polygenic modification score to determine the degree to which residual age at onset is better accounted for by a composite genetic score that includes many nominally associated SNPs. Overall, the effect sizes of 61 independent SNPs (only rs 1799977 was used to represent 3p22.2) in the GWA data and in the replication samples were not significantly different (sign test p-value, 0.609 ). Based upon effect sizes of SNPs estimated from the GWA analysis as a training set, a polygenic modification score was calculated for each of the 3,314 individuals in the Fluidigm data set. Then, residual age at onset was modeled as a function of polygenic modification score from the Fluidigm data. All 61 independent SNPs (one SNP for chromosome 3 and 60 other independent SNPs) were significant in the original GWA data (nominal p-value $<0.05$ ) (Table S2), and the subsequently derived polygenic modification score explained a nominally significant amount of the variance in residual age at onset of the Fluidigm samples (p-value, 0.0157). Although somewhat biased, the polygenic modification score based on the Fluidigm samples (using SNPs with nominal p -value $<0.05$ ) was highly significant in accounting for residual age at onset in HD subjects in the GWA data (p-value, 4.0E-26). When those missing genotypes in the Fluidigm test data set were assigned an expected genotype based upon allele frequency, the modification score became slightly more significant (Table S4), suggesting that missing genotypes and the smaller
size of test sample might have contributed to sub-optimal performance of the polygenic modification score in the Fluidigm data test set. Therefore, in order to judge the explanatory power of the polygenic modification score, we combined the GWA and Fluidigm data, and evenly split the data at random 1,000 times to generate training sets and corresponding test sets. Polygenic modification scores were then based on SNPs that passed pre-specified p-value thresholds in the training data: $0.05,0.01,0.001,0.0001$, and 0.00001 . As summarized in Figure 2, the polygenic modification score became more significant and predictive as more SNPs were used to calculate individual polygenic modification score in the test samples. The top SNP alone explained approximately $1.3 \%$ of variance in residual age at onset (Figure 2). However, the polygenic modification score, representing the genetic predisposition to deviate from the expected age at onset for a given CAG repeat size, was yet more predictive. Polygenic modification scores based on SNPs with p-values smaller than $0.05,0.01,0.001,0.0001$, and 0.00001 in the training samples (Figure S7), explained approximately 5.3, 3.9, 2.8, 2.4, and 2.3\% of the variance in residual age at onset of the test samples, respectively. The substantially increased R -squared values by polygenic modification score support the notion that HD onset can be modified by many genes with small effect sizes, even though the SNPs tagging those genes are not by themselves genome-wide significant in the current data sets. To evaluate the total amount of variance in residual age at onset explained by all SNPs collectively, we performed GCTA analysis using all QC-passed SNPs in the GWA data. The SNPs collectively explained approximately $20 \%$ of the variance in residual age at onset. Notably, $18 \%$ of the variance is due to SNPs other than those in the top chromosome 15 region, as revealed by exclusion of the chromosome 15 modifier signals from the analysis. The reported GWA analysis therefore did not have sufficient power to discover all of the genetic
variation that modifies HD onset, arguing for continuation of this strategy with the largest achievable sample size.

## Discussion

In summary, with candidate genotyping of HD individuals we have confirmed HD modifier loci on chromosomes 8 and 15 and identified the MLH1 region of chromosome 3 as an additional genome-wide significant modifier locus, while polygenic modification score analyses suggest that increasing the sample size of the GWA could identify yet more loci. The chromosome 3 modifier locus highlights $M L H 1$, involved in brain tissue CAG instability in Htt knock-in mice (14), consistent with the hypothesis that a functional impact of genetic variation in the modifier haplotype, via effects on CAG instability in the brains of HD patients, may alter CAG repeat size and thereby affect the rate of the disease process (13). This hypothesis is supported by the results of our GWA pathways analysis, which highlighted biological processes related to DNA maintenance (11). The functional variation within the modifier haplotype is associated with a delay in age at onset of 0.7 years, possibly consistent with an MLH1 hypomorphic variant that reduces somatic expansion of the CAG repeat due to reduced MLH1 activity. In any event, the impact of the functional variation on $M L H 1$ is likely to be subtle, as complete loss of function of the allele would be expected to predispose to Lynch Syndrome. The correspondence between GWA significance and eQTL results for SNPs across the region also raises the possibility that a potential regulatory effect on LRRFIP2 also contributes, either directly or indirectly via a coincident effect on MLH1, to the observed delay in onset. Clearly additional genetic and molecular analyses will be required to test the effects of the modifier haplotype and the mechanism by which it delays the rate of HD pathogenesis. Finally, our finding that a substantial amount of variation in HD age at
onset can be accounted for by genetic modification suggests that expanded GWA analysis with more subjects and therefore greater power could reveal additional modifier loci and biological networks of genes that offer bona fide therapeutic targets, validated in humans that influence the HD disease process.

## Materials and Methods

## Genotyping and quality control analysis

Selection of SNPs based on the recently completed GWA analysis (11) involved choosing the most significant SNPs amenable to genotyping on the Fluidigm platform for each of the top 61 independent modifier signals. Genotyping of 67 SNPs, representing 61 independent signals, was performed by the Genomics Platform at the Broad Institute on an independent HD cohort of 3,314 HD subjects from the European Huntington's Disease Network Registry Study. All SNPs had genotyping call rate greater than $90 \%$ and Hardy-Weinberg equilibrium p-value greater than 0.01 . Non-independent SNPs with lower call rates were excluded from the polygenic modification score analysis. The study was approved by the Institutional Review Board of Partners HealthCare and all subjects provided informed consent for participation in HD research.

## Residual age at motor diagnosis as a phenotype for association analysis

Age at onset of motor signs was based on rater estimation where available (1,443 subjects). In the absence of a rater estimate, we used age at onset data provided by family members ( 63 subjects) or patients ( 1,808 subjects). Predicted onset age was based on a phenotypic regression model describing the relationship between CAG repeat on the expanded chromosome and recorded age
at onset (6). Predicted age at onset was subtracted from observed age at onset to calculate the residual age at onset of motor signs, whose deviation from expectation represents the individual HD patient's level of modification of age at onset. For stringent replication analysis, we analyzed HD subjects with 40-55 CAG repeats with residual age at onset values within the range of the initial GWA data; since the most extreme data points have a greater potential for representing data entry or transcription errors, we excluded 5 subjects with extreme onset residuals beyond the range seen in the original GWA (Figure S1).

## Association analysis, meta-analysis, conditional analysis, and extreme dichotomous analysis

 In the Fluidigm data set, residual age at onset was modeled as function of a test SNP (additive model) and sex using a linear regression model. Main effect for sex was not significant in any association models. The small number of SNPs chosen for Fluidigm typing for the replication study were not sufficiently informative to distinguish sub-populations (data not shown). However, we reasoned that the discovery data set and replication data set have similar characteristics in terms of ancestry because of most individuals were from European countries. In addition, comparison of allele frequencies of replication SNPs in discovery and replication data sets revealed highly strong positive correlation (Figure S2), suggesting overall ancestry similarities between the two data sets. Subsequently, meta-analysis was performed by combining previous GWA results (11) and the current association results using the METAL program (http://genome.sph.umich.edu/wiki/METAL_Documentation) (33). Genome-wide significance was judged by meta-analysis p-value of 5E-8. To evaluate independence of chromosome 3 SNPs, GWA data and Fluidigm data were combined to perform conditional analyses. Briefly, residual age at onset was modeled as a function of either 1) rs1799977, 2) rs116483964, and 3) rs1799977and rs116483964 together. Fixed effect linear regression models with sex covariate were constructed for conditional analysis. In addition, for chromosome 3 SNPs, we combined GWA data and Fluidigm data to perform combined extreme dichotomous analysis in which data were sorted based on the residual age at onset phenotype, and samples with the top and bottom $20 \%$ residual age at onset values were extracted ( 1,478 samples in each group). Logistic regression analysis was performed using extreme dichotomous phenotype as the dependent variable, a SNP as a primary continuous independent variable and sex as a covariate.

## Capture sequencing analysis

Based on GWA analysis results, we chose 7 individuals who carry two minor alleles for the Chr3 top GWA SNP (i.e., rs144287831) with residual age at onset greater than 4 years. Since conditional analysis suggested the top SNP tags a single modifier chromosome, chosen HD subjects were hypothesized to carry two copies of the modifier haplotype. Design of capture probes was based on the Agilent's SureDesign online tool (https://earray.chem.agilent.com/suredesign/). A genomic region chr3:36,832,273-37,603,667 (hg19) was chosen in the SureDesign website in order to obtain ultra-long 120-mer biotinylated RNA bait probes that cover each site in the target region 5 times. To capture the entire genomic region including repeat sequences, we implemented an iterative capture probe design method. First, we input the chr3:36,832,273-37,603,667 as one contiguous region in the SureDesign website for most stringent probe design, generating 27,364 capture probes covering $63.9 \%$ of the target region. The most stringent condition will exclude repeat sequences based on repeat annotations such as RepeatMasker (http://www.repeatmasker.org/), WindowMasker (34), and Duke Uniqueness 35 (http://genome.ucsc.edu/cgi-bin/hgTrackUi?db=hg18\&g=wgEncodeMapability). Secondly, un-
captured regions (663 fragmented regions) from the previous design were fed into the program again for moderate stringent design, generating 8,794 capture probes covering $48.13 \%$ of the target region. Thirdly, remaining uncaptured regions (7,272 regions) were fed into the program for least stringent probe design, generating 14,544 probes (covering $89.79 \%$ of the target region). Lastly, remaining regions were used for probe design without any stringency (3,276 probes covering $100 \%$ of target region). Thus, repeat sequences are likely to be captured by probes designed based on no stringency. In order to focus on unique sequence but still capture the entire region, we replicated probe sets designed by most, moderate, and least stringent parameters. Target DNA capture/enrichment was based on the SureSelect method (SureSelect XT2 Target Enrichment System) (35). Briefly, each genomic DNA sample was sheared to produce smaller fragments, and indexed for multiplexing. Subsequently, pooled indexed DNA was hybridized with capture probes, and DNA-probe complexes were pulled down using magnetic streptavidin beads. Enriched multiplexed libraries were sequenced for 100 bp paired-end sequencing using Illumina HiSeq at the Broad Institute. Mean per base coverage was 174.7; $94.0 \%$ and $97.4 \%$ of the region has at least 10 X and 5 X coverages, respectively. Sequencing data were then analyzed using the Genome Analysis Toolkit (https://software.broadinstitute.org/gatk/). We followed the Best Practices workflow to perform quality control analysis, variant discovery, and genotype calling (36).

## Comparison of HD GWA modification signals to tissue eQTL signals

To determine whether modification of HD captured by significant chromosome 3 SNPs might be mediated by differential expression levels of genes in the region, we compared GWA association signals to HaploReg, GTEx eQTL data, and BRAINEAC exon level eQTL data. Initially, we counted the number of tissues in which a test SNP and a test gene were significantly associated
using HaploReg web resources, which annotated GTEx and other eQTL data sets. Due to potential tissue-specific regulation of gene expression, directions of eQTLs were not considered. Subsequently, we evaluated the patterns of correlation between modifier GWA significances and the number of significant tissues for each corresponding SNP. Next, we analyzed GTEx data focusing on brain regions and two candidate genes, MLH1 and LRRFIP2. Cortex, caudate, putamen and cerebellum in GTEx data were analyzed to evaluate correspondence between tissuespecific cis eQTL signals and HD modification signals. Focusing on MLH1 and LRRFIP2 in putamen, exon array expression data from BRAINEAC were analyzed to test eQTL association with SNPs in the region, and subsequently eQTL signals were compared to HD GWA modifier association signals. Mapping of SNPs in eQTL data and HD GWA data was based on genomic coordinates (hg19 assembly).

## Polygenic modification score analysis

In order to determine the explanatory power of a polygenic modification score in explaining the individual deviation from the expected age at onset for a given CAG size, we 1) obtained effect sizes and significances of SNPs from the initial GWA analysis (11), 2) calculated a modification score for the individual test sample (Fluidigm data) by summing the products of test SNP allele counts and corresponding effect sizes (http://zzz.bwh.harvard.edu/plink/profile.shtml), and 3) performed linear regression analysis by modeling residual age at onset of the test samples as a function of the polygenic modification score. The same procedure was applied for polygenic modification score analysis using Fluidigm data as a training set and GWA data as a test set. Only independent SNPs were used in this analysis. When SNPs were not independent (based on conditional analysis in the initial GWA data), the SNP with the highest genotyping call rate in the

Fluidigm data was chosen to represent the association signal in the region; 61 independent SNPs were used to drive polygenic modification scores of test samples. Chromosome 3 p22.2 was represented by rs1799977. Among the 61 independent SNPs, all of which were associated (p-value $<0.05$ ) with residual age at onset in the GWA data, 7 were associated (nominal p-value $<0.05$ ) in the Fluidigm data. Missing genotypes in the Fluidigm test samples were ignored. Additionally, we also performed polygenic modification score analysis based on imputed Fluidigm test data by assigning expected genotypes based on allele frequency in the Fluidigm data. For a given missing SNP site in an individual, expected genotype in the dosage format was calculated by multiplying allele frequency of that SNP in the replication data set by 2 as described in the PLINK program manual (http://zzz.bwh.harvard.edu/plink/profile.shtml). The polygenic modification score was then calculated for each individual in the test samples to be used as a predictor variable of a linear regression model to explain residual age at onset of test samples. Polygenic modification score was defined as the mean of effect size of a minor allele X minor allele count based on non-missing SNPs.

## Polygenic modification score analysis based on randomly chosen training and test samples

## from the combined data

Our Fluidigm validation data set had missing data. Missing data in the test samples may reduce the accuracy of polygenic modification score when ignored or expected genotypes were assigned. To objectively evaluate the power of polygenic modification score, we 1) combined the GWA data and Fluidigm data, 2) randomly and evenly split into training samples (3,698 samples) and test samples (3,698 samples), 3) performed association analysis using genotype and residual age at onset of training samples, 4) calculated polygenic modification score of test samples based on
effect size estimation from the training sample analysis and allele count of test samples, and 5) evaluated the significance of the polygenic modification score in explaining residual age at onset of test samples. This procedure was repeated 1,000 times to obtain unbiased estimations. Missing genotype data in the test samples were excluded from calculating the polygenic modification score. Scoring SNPs were based on association p-value of $0.05,0.01,0.001,0.0001$, and 0.00001 in the training samples. All SNPs were used as scoring SNPs as long as they passed the pre-specified significance thresholds.

## GCTA analysis

The overall genetic contribution to residual age at onset was calculated by the GCTA (Genomewide Complex Trait Analysis) program. Briefly, GWA data were analyzed by the restricted maximum likelihood (REML) method using the following parameters: --grm-adj, 0 and --grmcutoff, 0.025 . For standard GCTA analysis, all QC-passed SNPs in the GWA data were analyzed. The chromosome $15: 31,105,000-31,315,000$ region harbors two independent genome-wide significant modification signals (11). Therefore, this region was excluded from the GWA data to estimate the contribution of the chromosome 15 region to modification of age at onset.

## Genomic coordinates

GRCh37/hg19 was used.

## Acknowledgements

This work was supported by the CHDI Foundation, National Institutes of Health (USA; P50NS016367, U01NS082079, R01NS091161 and R01NS049206), and Medical Research

Council (UK; G0801418 and MR/L010305/1). European Huntington's Disease Network Registry Investigators who provided HD patient samples and data are listed in the Supplemental Material. .

## Conflict of Interest Statement

None of the authors declares a conflict of interest

## References

1. Huntington's Disease Collaborative Research Group. (1993) A novel gene containing a trinucleotide repeat that is expanded and unstable on Huntington's disease chromosomes. Cell, 72, 971-983.
2. Keum, J.W., Shin, A., Gillis, T., Mysore, J.S., Abu Elneel, K., Lucente, D., Hadzi, T., Holmans, P., Jones, L., Orth, M. et al. (2016) The HTT CAG-Expansion Mutation Determines Age at Death but Not Disease Duration in Huntington Disease. Am. J. Hum. Genet., 98, 287-298. 3. Bates, G.P., Dorsey, R., Gusella, J.F., Hayden, M.R., Kay, C., Leavitt, B.R., Nance, M., Ross, C.A., Scahill, R.I., Wetzel, R. et al. (2015) Huntington disease. Nat. Rev. Dis. Primers, 1, 15005.
3. Andrew, S.E., Goldberg, Y.P., Kremer, B., Telenius, H., Theilmann, J., Adam, S., Starr, E., Squitieri, F., Lin, B., Kalchman, M.A. et al. (1993) The relationship between trinucleotide (CAG) repeat length and clinical features of Huntington's disease. Nat. Genet., 4, 398-403.
4. Duyao, M., Ambrose, C., Myers, R., Novelletto, A., Persichetti, F., Frontali, M., Folstein, S., Ross, C., Franz, M., Abbott, M. et al. (1993) Trinucleotide repeat length instability and age of onset in Huntington's disease. Nat. Genet., 4, 387-392.
5. Lee, J.M., Ramos, E.M., Lee, J.H., Gillis, T., Mysore, J.S., Hayden, M.R., Warby, S.C., Morrison, P., Nance, M., Ross, C.A. et al. (2012) CAG repeat expansion in Huntington disease determines age at onset in a fully dominant fashion. Neurology, 78, 690-695.
6. Persichetti, F., Srinidhi, J., Kanaley, L., Ge, P., Myers, R.H., D'Arrigo, K., Barnes, G.T., MacDonald, M.E., Vonsattel, J.P., Gusella, J.F. et al. (1994) Huntington's disease CAG trinucleotide repeats in pathologically confirmed post-mortem brains. Neurobiol. Dis., 1, 159-166.
7. Snell, R.G., MacMillan, J.C., Cheadle, J.P., Fenton, I., Lazarou, L.P., Davies, P., MacDonald, M.E., Gusella, J.F., Harper, P.S. and Shaw, D.J. (1993) Relationship between trinucleotide repeat expansion and phenotypic variation in Huntington's disease. Nat. Genet., 4, 393-397.
8. Gusella, J.F., MacDonald, M.E. and Lee, J.M. (2014) Genetic modifiers of Huntington's disease. Mov. Disord., 29, 1359-1365.
9. Wexler, N.S., Lorimer, J., Porter, J., Gomez, F., Moskowitz, C., Shackell, E., Marder, K., Penchaszadeh, G., Roberts, S.A., Gayan, J. et al. (2004) Venezuelan kindreds reveal that genetic and environmental factors modulate Huntington's disease age of onset. Proc. Natl. Acad. Sci. U. S. A., 101, 3498-3503.
10. Genetic Modifiers of Huntington's Disease Consortium. (2015) Identification of genetic factors that modify clinical onset of Huntington's Disease. Cell, 162, 516-526.
11. Pal, T., Permuth-Wey, J. and Sellers, T.A. (2008) A review of the clinical relevance of mismatch-repair deficiency in ovarian cancer. Cancer, 113, 733-742.
12. Swami, M., Hendricks, A.E., Gillis, T., Massood, T., Mysore, J., Myers, R.H. and Wheeler, V.C. (2009) Somatic expansion of the Huntington's disease CAG repeat in the brain is associated with an earlier age of disease onset. Hum. Mol. Genet., 18, 3039-3047.
13. Pinto, R.M., Dragileva, E., Kirby, A., Lloret, A., Lopez, E., St Claire, J., Panigrahi, G.B., Hou, C., Holloway, K., Gillis, T. et al. (2013) Mismatch repair genes Mlh1 and Mlh3 modify CAG instability in Huntington's disease mice: genome-wide and candidate approaches. PLoS Genet., 9, e1003930.
14. Correia, K., Harold, D., Kim, K.H., Holmans, P., Jones, L., Orth, M., Myers, R.H., Kwak, S., Wheeler, V.C., MacDonald, M.E. et al. (2015) The Genetic Modifiers of Motor OnsetAge
(GeM MOA) Website: Genome-wide Association Analysis for Genetic Modifiers of Huntington's Disease. J. Huntingtons Dis., 4, 279-284.
15. Baker, S.M., Plug, A.W., Prolla, T.A., Bronner, C.E., Harris, A.C., Yao, X., Christie, D.M., Monell, C., Arnheim, N., Bradley, A. et al. (1996) Involvement of mouse Mlh1 in DNA mismatch repair and meiotic crossing over. Nat. Genet., 13, 336-342.
16. Guerrette, S., Acharya, S. and Fishel, R. (1999) The interaction of the human MutL homologues in hereditary nonpolyposis colon cancer. J. Biol. Chem., 274, 6336-6341.
17. Liu, J., Bang, A.G., Kintner, C., Orth, A.P., Chanda, S.K., Ding, S. and Schultz, P.G. (2005) Identification of the Wnt signaling activator leucine-rich repeat in Flightless interaction protein 2 by a genome-wide functional analysis. Proc. Natl. Acad. Sci. U. S. A., 102, 1927-1932.
18. Pinheiro, M., Pinto, C., Peixoto, A., Veiga, I., Mesquita, B., Henrique, R., Baptista, M., Fragoso, M., Sousa, O., Pereira, H. et al. (2011) A novel exonic rearrangement affecting MLH1 and the contiguous LRRFIP2 is a founder mutation in Portuguese Lynch syndrome families. Genet. Med., 13, 895-902.
19. Talkowski, M.E., Ernst, C., Heilbut, A., Chiang, C., Hanscom, C., Lindgren, A., Kirby, A., Liu, S., Muddukrishna, B., Ohsumi, T.K. et al. (2011) Next-generation sequencing strategies enable routine detection of balanced chromosome rearrangements for clinical diagnostics and genetic research. Am. J. Hum. Genet., 88, 469-481.
20. Chiang, C., Jacobsen, J.C., Ernst, C., Hanscom, C., Heilbut, A., Blumenthal, I., Mills, R.E., Kirby, A., Lindgren, A.M., Rudiger, S.R. et al. (2012) Complex reorganization and predominant non-homologous repair following chromosomal breakage in karyotypically balanced germline rearrangements and transgenic integration. Nat. Genet., 44, 390-397.
21. Peng, H.X., Xu, X., Yang, R., Chu, Y.M., Yang, D.M., Xu, Y., Zhou, F.L., Ma, W.Z., Zhang, X.J., Guan, M. et al. (2016) Molecular analysis of MLH1 variants in Chinese sporadic colorectal cancer patients. Genet. Mol. Res., 15, gmr. 15027689.
22. Santibanez Koref, M., Wilson, V., Cartwright, N., Cunnington, M.S., Mathers, J.C., Bishop, D.T., Curtis, A., Dunlop, M.G. and Burn, J. (2010) MLH1 Differential allelic expression in mutation carriers and controls. Ann. Hum. Genet., 74, 479-488.
23. An, Y., Jin, G., Wang, H., Wang, Y., Liu, H., Li, R., Wang, H., Qian, J., Sun, W., Wang, Y. et al. (2008) Polymorphisms in hMLH1 and risk of early-onset lung cancer in a southeast Chinese population. Lung Cancer, 59, 164-170.
24. Chen, H., Shen, Z., Hu, Y., Xiao, Q., Bei, D., Shen, X. and Ding, K. (2015) Association between MutL homolog 1 polymorphisms and the risk of colorectal cancer: a meta-analysis. $J$. Cancer Res. Clin. Oncol., 141, 2147-2158.
25. Langeberg, W.J., Kwon, E.M., Koopmeiners, J.S., Ostrander, E.A. and Stanford, J.L. (2010) Population-based study of the association of variants in mismatch repair genes with prostate cancer risk and outcomes. Cancer Epidemiol. Biomarkers Prev., 19, 258-264.
26. Mann, A., Hogdall, E., Ramus, S.J., DiCioccio, R.A., Hogdall, C., Quaye, L., McGuire, V., Whittemore, A.S., Shah, M., Greenberg, D. et al. (2008) Mismatch repair gene polymorphisms and survival in invasive ovarian cancer patients. Eur. J. Cancer, 44, 2259-2265.
27. Nejda, N., Iglesias, D., Moreno Azcoita, M., Medina Arana, V., Gonzalez-Aguilera, J.J. and Fernandez-Peralta, A.M. (2009) A MLH1 polymorphism that increases cancer risk is associated with better outcome in sporadic colorectal cancer. Cancer Genet. Cytogenet., 193, 7177.
28. Niu, L., Li, S., Liang, H. and Li, H. (2015) The hMLH1-93G>A Polymorphism and Risk of Ovarian Cancer in the Chinese Population. PLoS One, 10, e0135822.
29. Picelli, S., Zajac, P., Zhou, X.L., Edler, D., Lenander, C., Dalen, J., Hjern, F., Lundqvist, N., Lindforss, U., Pahlman, L. et al. (2010) Common variants in human CRC genes as low-risk alleles. Eur. J. Cancer, 46, 1041-1048.
30. Rossi, D., Rasi, S., Di Rocco, A., Fabbri, A., Forconi, F., Gloghini, A., Bruscaggin, A., Franceschetti, S., Fangazio, M., De Paoli, L. et al. (2011) The host genetic background of DNA repair mechanisms is an independent predictor of survival in diffuse large B-cell lymphoma. Blood, 117, 2405-2413.
31. Sapkota, Y., Mackey, J.R., Lai, R., Franco-Villalobos, C., Lupichuk, S., Robson, P.J., Kopciuk, K., Cass, C.E., Yasui, Y. and Damaraju, S. (2014) Assessing SNP-SNP interactions among DNA repair, modification and metabolism related pathway genes in breast cancer susceptibility. PLoS One, 8, e64896.
32. Willer, C.J., Li, Y. and Abecasis, G.R. (2010) METAL: fast and efficient meta-analysis of genomewide association scans. Bioinformatics, 26, 2190-2191.
33. Morgulis, A., Gertz, E.M., Schaffer, A.A. and Agarwala, R. (2006) WindowMasker: window-based masker for sequenced genomes. Bioinformatics, 22, 134-141.
34. Gnirke, A., Melnikov, A., Maguire, J., Rogov, P., LeProust, E.M., Brockman, W., Fennell, T., Giannoukos, G., Fisher, S., Russ, C. et al. (2009) Solution hybrid selection with ultra-long oligonucleotides for massively parallel targeted sequencing. Nat. Biotechnol., 27, 182-189.
35. Van der Auwera, G.A., Carneiro, M.O., Hartl, C., Poplin, R., Del Angel, G., LevyMoonshine, A., Jordan, T., Shakir, K., Roazen, D., Thibault, J. et al. (2013) From FastQ data to
high confidence variant calls: the Genome Analysis Toolkit best practices pipeline. Curr. Protoc.
Bioinformatics, 43, 11.10.11-11.10.33.

## Figure Legends

## Figure 1. Summary of meta-analysis for the chromosome 3 locus.

A. GWA analysis results are shown as open grey circles, except the top SNPs shown as black circles. For two of the latter, Fluidigm genotyping data was generated on an independent study sample and subsequent meta-analysis revealed genome-wide significance for both SNPs (filled red circles). Arrows show the levels of improvement by addition of Fluidigm data. X -axis and Y -axis denote genomic coordinates (hg19 assembly) and significance of association, respectively. A line in cyan represents the recombination rate based on HapMap data (secondary Y-axis). A red dashed horizontal line marks the level of genome-wide significance, and a blue horizontal line indicates the region that was analyzed by capture sequencing analysis. All exons of transcripts (RefSeq) representing the same gene were combined to represent each gene in this region. Genes in red and blue denote genes on plus and minus strand, respectively. A red horizontal bar indicates a region expanded in panel B.
B. Expanded region denoted by the red horizontal bar in Panel A. Filled black circles, filled grey circles, and open grey circles represent SNPs with allele frequencies between 31 and $32 \%$, higher than $32 \%$, and below $31 \%$, respectively. IDs of SNPs with minor allele frequency between 31 and $32 \%$ are shown. This region harbors exons of various transcripts from the 3' portion of MLH1 (red) and the 5' portion of LRRFIP2 (blue). Representative transcripts with different exons in this region were obtained from RefSeq and UCSC Genome Browser.

Figure 2. Increased explanatory power of the polygenic modification score.
Combined data were randomly split into a training and test set of equal size to perform polygenic modification score analysis. For a given split, polygenic modification score in the test samples was calculated based on independent SNPs with training set p-value smaller than 0.05 (purple), 0.01 (red), 0.001 (green), 0.0001 (blue) or 0.00001 (orange). Then, linear regression analysis was performed by modeling residual age at onset of test samples as a function of polygenic modification scores based on multiple SNPs with different levels of training set association analysis p-value. For each iteration, we recorded p-value and R -square value of the polygenic modification score. The main plot in the center shows significance ( Y -axis) and percent R -squared values of polygenic modification score. Histograms on the top and on the right side of the main plot show the distributions of R-squared and significance values, respectively. As a reference, significance and R-squared value of the model based on the single most significant SNP are shown in grey.

1

2

6 slope estimation, respectively.
$7 \quad \$$ Genes represent nearest genes, not necessarily causal modifier genes.

Table 2. Extreme dichotomous analysis and conditional analysis of chromosome 3 SNPs*

| A. Dichotomous analysis |  |
| :--- | :---: |
| Test SNP | p-value |
| rs1799977 | $5.3 \mathrm{E}-09$ |
| rs116483964 | $5.6 \mathrm{E}-09$ |


| B. Conditional analysis |  |
| :--- | :---: |
| Test SNP | p-value |
| rs1799977 | $9.5 \mathrm{E}-09$ |
| rs116483964 | $6.2 \mathrm{E}-09$ |
| rs1799977 conditioned by rs116483964 | 0.9818 |
| rs116483964 conditioned by rs1799977 | 0.5145 |

* For dichotomous analysis, extreme late and extreme early groups (1,478 samples for each group) comprising top and bottom $20 \%$ of subject based on samples sorted by residual age at onset in a descending order were identified from combined data set (GWA data + Fluidigm data). Then, logistic regression analysis was performed for each SNP using the test SNP as the main predictor variable and sex as a covariate. For conditional analysis, GWA data and Fluidigm data were combined to perform fixed effect model linear regression analysis to determine independence of the two SNPs. Two SNPs were used simultaneously as independent variables in a linear regression model, and corresponding p-values are obtained. For extreme dichotomous phenotype analysis, 2 subsets of data were extracted from the combined data set based on residual age at onset phenotype.

1 Table 3. Modifier haplotype defined by top-scoring SNPs*

| SNP | Chr 3 bp <br> (hg19) | minor <br> allele | major <br> allele | MAF <br> All <br> samples | MAF <br> 1st AO <br> residual <br> quartile | MAF <br> 2nd AO <br> residual <br> quartile | MAF <br> 3rd AO <br> residual <br> quartile | MAF <br> 4th AO <br> residual <br> quartile | P-value <br> quantitative <br> analysis of AO <br> residual | P -value dichotomous analysis of AO residual $20 \%$ extremes |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| rs1799977 | 37,053,568 | G | A | 0.319 | 0.279 | 0.298 | 0.324 | 0.351 | 7.2E-07 | 2.7E-06 |
| rs144287831 | 37,068,079 | C | T | 0.312 | 0.279 | 0.297 | 0.322 | 0.350 | 2.2E-07 | 1.5E-06 |
| rs141716664 | 37,078,200 | T | - | 0.315 | 0.281 | 0.299 | 0.323 | 0.350 | 4.4E-07/ | 3.5E-06 |
| rs116483964 | 37,102,696 | A | G | 0.320 | 0.279 | 0.296 | 0.322 | 0.351 | 4.0E-07 | 2.1E-06 |
| rs148648107 | 37,118,345 | A | G | 0.318 | 0.280 | 0.297 | 0.323 | 0.350 | $9.6 \mathrm{E}-07$ | 4.3E-06 |
| rs11714838 | 37,121,844 | A | G | 0.318 | 0.281 | 0.297 | 0.323 | 0.352 | 1.3E-06 | 5.0E-06 |
| rs147891316 | 37,131,815 | T | G | 0.317 | 0.280 | 0.297 | 0.323 | 0.351 | 1.1E-06 | 7.8E-06 |

*Allele frequencies of SNPs in GWA data were analyzed to localize functional variation. Subjects in GWA analysis were grouped into quartile bins based on their residual age at onset; 1st and 4th AO residual quartiles represent earliest and latest age at onset groups, respectively. Then, minor allele frequencies of SNPs were calculated for each quartile bin to understand how alleles are distributed relative to residual age at onset phenotype. MAF means minor allele frequency. P-value quantitative analysis of AO residual represents the p-value in the original GWA analysis. P-value dichotomous analysis of AO residual $20 \%$ extremes represent p -values

7 from the logistic analysis of GWA data.

Abbreviations"
Chr: chromosome
EHDN: European Huntington's Disease Network
eQTL: expression Quantitative Trait Locus
GCTA: Genome-wide Complex Trait Analysis
GWA: Genome-wide Association
HD: Huntington's Disease
MAF: minor allele frequency
QC: quality control
SNP: single nucleotide polymorphism

## Supplemental Tables

Table S1-Genotype of replication samples
See excel file TableS1.xls

Table S2. SNPs analyzed in replication samples and for polygenic modification score See excel file TableS2.xls

Table S3. Consensus alleles of the effect haplotype. *

|  |  |  |  | Number <br> of |  |  |
| :--- | ---: | :--- | :--- | :--- | :--- | :--- |
| SNP ID | Chromosome | BP (hg19) | Reference allele | Alternative | allele | Consensus <br> consensus <br> allele |
| rs4647224 | 3 | $37,043,230$ | G | A | A | 14 |
| rs59335282 | 3 | $37,043,443$ | GT | G | G | 14 |
| rs28393182 | 3 | $37,043,459$ | T | G | G | G |


| rs143397020 | 3 | 37,068,331 | GAATAATAAT | G | G | 14 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| rs9852810 | 3 | 37,068,969 | G | A | A | 14 |
| rs11719992 | 3 | 37,069,872 | T | G | G | 14 |
| rs2286940 | 3 | 37,070,106 | C | T | T | 14 |
| rs3774335 | 3 | 37,072,627 | A | C | C | 14 |
| rs3774334 | 3 | 37,072,705 | G | A | A | 14 |
| rs9819025 | 3 | 37,073,287 | T | G | G | 14 |
| rs6765395 | 3 | 37,073,579 | T | G | G | 14 |
| rs3821826 | 3 | 37,074,368 | C | G | G | 14 |
| rs997588 | 3 | 37,075,142 | G | A | A | 13 |
| rs6772548 | 3 | 37,075,934 | T | C | C | 14 |
| rs6784088 | 3 | 37,075,984 | A | G | G | 14 |
| rs6550447 | 3 | 37,078,280 | G | C | C | 14 |
| rs4678925 | 3 | 37,078,506 | A | G | G | 14 |
| rs748766 | 3 | 37,082,874 | T | C | C | 14 |
| rs9876116 | 3 | 37,083,740 | A | G | G | 14 |
| rs67401825 | 3 | 37,085,970 | T | C | C | 14 |
| rs9822082 | 3 | 37,086,204 | G | A | A | 14 |
| rs75839046 | 3 | 37,086,416 | A | G | A | 12 |
| rs184308009 | 3 | 37,087,179 | T | C | T | 12 |
| rs9831178 | 3 | 37,087,417 | C | T | T | 14 |
| rs11926842 | 3 | 37,088,102 | A | T | T | 14 |
| rs1 1290150 | 3 | 37,089,840 | CT | C | C | 14 |
| rs2241031 | 3 | 37,090,274 | C | T | T | 14 |
| rs1860968 | 3 | 37,091,325 | G | A | A | 14 |
| rs1558529 | 3 | 37,093,064 | T | C | C | 14 |
| rs4579 | 3 | 37,094,679 | G | A | A | 14 |
| rs10849 | 3 | 37,095,070 | C | T | T | 14 |
| rs4678932 | 3 | 37,096,303 | T | G | G | 14 |
| rs2110194 | 3 | 37,097,087 | C | T | T | 14 |


| rs2363499 | 3 | 37,097,546 | A | G | G | 14 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| rs202119305 | 3 | 37,097,949 | CT | C | C | 14 |
| rs143498278 | 3 | 37,098,064 | C | T | C | 10 |
| rs58257408 | 3 | 37,099,025 | CT | C | C | 14 |
| rs3774327 | 3 | 37,099,367 | G | A | A | 14 |
| rs3774326 | 3 | 37,099,566 | G | A | A | 14 |
| rs7639327 | 3 | 37,099,788 | A | G | G | 14 |
| rs202036094 | 3 | 37,100,166 | CAAA | C | C | 14 |
| rs7372653 | 3 | 37,101,079 | G | A | A | 14 |
| rs11720064 | 3 | 37,101,519 | G | T | T | 14 |
| rs139922612 | 3 | 37,102,458 | AGTGC | A | A | 14 |
| rs58693636 | 3 | 37,102,623 | C | T | T | 14 |
| rs1 16483964 | 3 | 37,102,696 | G | A | A | 14 |
| rs145261675 | 3 | 37,102,874 | CTTTTCT | C | C | 14 |
| rs6808735 | 3 | 37,104,246 | A | C | C | 14 |
| rs2058476 | 3 | 37,104,896 | G | T | T | 14 |
| rs1468712 | 3 | 37,106,013 | T | C | C | 14 |
| rs1468713 | 3 | 37,106,115 | A | G | G | 14 |
| rs7639375 | 3 | 37,107,022 | C | A | A | 14 |
| rs2302503 | 3 | 37,107,470 | G | A | A | 14 |
| rs6550448 | 3 | 37,108,896 | T | A | A | 14 |
| rs56180213 | 3 | 37,109,633 | C | A | A | 14 |
| rs9823428 | 3 | 37,111,130 | G | A | A | 14 |
| rs17810211 | 3 | 37,113,405 | T | C | C | 14 |
| rs3836485 | 3 | 37,115,313 | GC | G | G | 14 |
| rs1558527 | 3 | 37,115,658 | T | C | C | 14 |
| rs7651033 | 3 | 37,116,042 | C | T | T | 14 |
| rs2302504 | 3 | 37,116,386 | G | T | T | 14 |
| rs11709376 | 3 | 37,116,808 | C | G | G | 14 |
| rs726769 | 3 | 37,117,741 | A | G | G | 14 |


| rs148648107 | 3 | 37,118,345 | G | A | A | 14 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| rs4678935 | 3 | 37,119,835 | A | C | C | 14 |
| rs9810355 | 3 | 37,121,074 | A | G | G | 14 |
| rs6806487 | 3 | 37,121,092 | C | T | T | 14 |
| rs6806861 | 3 | 37,121,293 | G | A | A | 14 |
| rs9814918 | 3 | 37,121,613 | A | G | G | 14 |
| rs11707197 | 3 | 37,122,329 | A | C | C | 14 |
| rs6550449 | 3 | 37,122,997 | A | G | G | 14 |
| rs6550450 | 3 | 37,123,099 | C | G | G | 14 |
| rs6550451 | 3 | 37,123,250 | G | A | A | 14 |
| rs1990492 | 3 | 37,124,620 | A | G | G | 14 |
| rs9846039 | 3 | 37,125,699 | C | T | T | 14 |
| rs1 13687377 | 3 | 37,127,076 | CT | C | C | 14 |
| rs3821824 | 3 | 37,130,942 | G | C | C | 14 |
| rs2302505 | 3 | 37,131,404 | C | T | T | 14 |
| rs147891316 | 3 | 37,131,815 | G | T | T | 14 |
| rs9879135 | 3 | 37,132,279 | G | A | A | 14 |
| rs113267946 | 3 | 37,132,719 | GA | G | G | 14 |
| rs2302506 | 3 | 37,133,124 | A | G | G | 14 |
| rs11915301 | 3 | 37,133,853 | G | A | A | 14 |
| rs3774323 | 3 | 37,134,451 | T | C | C | 14 |
| rs17204675 | 3 | 37,135,797 | T | C | C | 14 |
| rs9820888 | 3 | 37,136,711 | T | G | G | 14 |
| rs67385735 | 3 | 37,138,751 | A | G | G | 14 |
| rs5847949 | 3 | 37,139,597 | AT | A | A | 14 |
| rs7638252 | 3 | 37,141,732 | G | C | C | 14 |
| rs57588408 | 3 | 37,141,928 | CAT | C | C | 14 |
| rs7616160 | 3 | 37,141,977 | A | G | G | 14 |
| rs143418804 | 3 | 37,142,394 | T | C | T | 13 |
| rs571725354 | 3 | 37,064,415 | G | A | G | 13 |


| rs554553185 | 3 | $37,100,477$ | A | G | A | 13 |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| rs527583094 | 3 | $37,126,407$ | T | C | T | 13 |

* Seven HD individuals who carry two minor alleles for rs144287831 were captured to determine the sequence of Chr3:36,832,347-37,603,667 region. Variable sites and alternative alleles in 7 individuals were detected in the capture sequencing data, and consensus alleles among 14 chromosomes in this region were identified by taking the most frequent alleles for each site. Therefore, consensus alleles in this table represent either 1) reference or alternative alleles predominant in 14 chromosomes, or 2) alternative alleles present on all 14 chromosomes. For each site, the number of defined consensus allele $s$ was counted among 14 chromosomes. For example, 14 means all 14 chromosomes carry the consensus allele for a given site.

Table S4. Polygenic modification score analysis. *

| Analysis | Training <br> set | Test set | Score SNPs | Handling of missing <br> genotype in the test set | P-value |
| :---: | :---: | :---: | :---: | :---: | :---: |
| A | GWA | Fluidigm | p-value $<0.05$ in the <br> training set | Excluded | 0.0157 |
| B | Fluidigm | GWA | $(61$ independent <br> SNPs $)$ | No missing data in the <br> test set | $4.0 \mathrm{E}-26$ |
| C | GWA | Fluidigm | p-value $<0.05$ in the <br> training set | Expected genotype was <br> assigned based on <br> allele frequency | 0.0144 |

* Using 61 independent SNPs typed in the Fluidigm data, we performed polygenic modification score analysis.
A) GWA data were analyzed to estimate effect size of SNPs and to calculate p-values. Subsequently, the polygenic modification score of Fluidigm data based on SNPs with GWA analysis p -value smaller than 0.05 was calculated. Then, residual age at onset of Fluidigm samples was modeled as a function of polygenic modification score in a linear regression model to determine its explanatory power.
B) The same procedures were performed using Fluidigm data as a training set and GWA data as a test set.
C) The same SNPs as in analysis A were used to calculate the polygenic modification score of Fluidigm data imputed for missing genotype. For a missing site in a given individual, allele frequency of the minor allele multiplied by 2 was used as an expected genotype to calculate the polygenic modification score. The same analytical pipeline was used to determine the significance of the polygenic modification score.

Supplemental Figures


Figure S1. Residual age at onset phenotype of replication data.
Distribution of residual age at onset of replication samples (histogram in blue) was compared to that of GWA data (histogram in red) to visually confirm the homogeneity of phenotypes of replication samples and GWA samples.


Figure S2. Minor allele frequencies of test SNPs in the discovery and replication data sets For 61 SNPs we focused on for the replication analysis, minor allele frequencies in discovery set (GWA data; X-axis) and replication set (Fluidigm data; Y-axis) are compared.


Figure S3. Correspondence between GWA modification signals and cis eQTL signals.
To explore the molecular mechanisms of modification conferred by the chromosome 3 locus, we determined whether GWA modifier association signals were similar to eQTL signals in tissues. For a given gene, we counted the number of significant tissues associated with SNPs in the HaploReg annotation data base regardless of the effect sizes. Each gene was graphed using two plots. The plot on the left shows GWA association signal on the primary Y-axis (grey circles) and the number of tissues with significant eQTLs on the secondary Y-axis (black crosses) for all SNPs. For shared SNPs between our GWA data and HaploReg data base, significance (-log10pvalue) in GWA data (X-axis) were directly compared to the number of significant tissues (plot on the right).


Figure S 4. SNPs associated with expression levels of MLH1 and LRRFIP2 in brain subregions.

MLH1 and LRRFIP2 showed promising correspondence with cis eQTL signals. Subsequently, we evaluated the brain eQTL signals in GTEx data, and compared to our GWA modifier signals. Caudate (top left), putamen (top right), cortex (bottom left), and cerebellum (bottom right) were analyzed for eQTL data in GTEx data (version 6). Significance of SNPs is represented by $\log 10(p$-value $)$ on both axes.


Figure S 5. Relationship between cis eQTL signals for LRRFIP2 in putamen and GWA modification association signals in BRAINEAC data.

BRAINEAC data (http://www.braineac.org/) was analyzed to further evaluate the impacts of SNPs on mRNA expression levels of $M L H 1$ and LRRFIP2 in putamen. 129 putamen samples were analyzed in BRAINEAC. Expression levels of each region determined by BRAINEAC were modeled as a function of SNP in a linear regression analysis framework. Then, significances (i.e., $-\log 10(\mathrm{p}$-value) from eQTL analysis (Y-axis) were compared to significances from HD onset modifier GWA analysis (X-axis; - $\log 10(\mathrm{p}-\mathrm{valud})$ ). Most of exons of MLH1 or LRRFIP2 did not show trends of correlation between eQTL signals and GWA modifier association signals. However, eQTL signals for chr3:37 , 108,538-37,110,067 (A; 21st intron of LRRFIP2, NM_006309.3) and chr3:37 ,138,107-37,138,136 (B; 16th exon of LRRFIP2, NM_006309.3) in putamen weakly corresponded with modifier association signals.


Figure S6. Association of rs116483964 and rs1799977 with the expression levels of MLH1 and LRRFIP2 in brain regions. Expression levels of MLH1 (open symbols) and LRRFIP2 (filled symbols) in putamen (circle), caudate (square), cortex (diamond), and cerebellum (triangle) were compared against rs 1799977 in the GTEx data. The levels of cis eQTL significance of each SNP-gene pair in a given brain region (Y-axis) were plotted against corresponding normalized effect sizes (i.e., beta on X-axis). A vertical and a horizontal grey dashed line, respectively represent a slope of zero and nominal significance of 0.05 .

## European Huntington's Disease Network REGISTRY Study Investigators

Registry Steering committee: Anne-Catherine Bachoud-Lévi, Anna Rita Bentivoglio, Ida
Biunno, Raphael M Bonelli, Jean-Marc Burgunder, Stephen B Dunnett, Joaquim J Ferreira, Olivia J. Handley, Arvid Heiberg, Torsten Illmann, G Bernhard Landwehrmeyer, Jamie Levey, Maria A. Ramos-Arroyo, Jørgen E Nielsen, Susana Pro Koivisto, Markku Päivärinta, Raymund A.C. Roos, Ana Rojo Sebastián, Sarah J Tabrizi, Wim Vandenberghe, Christine VerellenDumoulin, Tereza Uhrova, Jan Wahlström, Jacek Zaremba

Language coordinators: Verena Baake, Katrin Barth, Monica Bascuñana Garde, Sabrina Betz, Reineke Bos, Jenny Callaghan, Adrien Come, Leonor Correia Guedes, Daniel Ecker, Ana Maria Finisterra, Ruth Fullam, Mette Gilling, Lena Gustafsson, Olivia J. Handley, Carina Hvalstedt, Christine Held, Kerstin Koppers, Claudia Lamanna, Matilde Laurà, Asunción Martínez Descals, Saül Martinez-Horta, Tiago Mestre, Sara Minster, Daniela Monza, Lisanne Mütze, Martin Oehmen, Michael Orth, Hélène Padieu, Laurent Paterski, Nadia Peppa, Susana Pro Koivisto, Martina Di Renzo, Amandine Rialland, Niini Røren, Pavla Šašinková, Erika Timewell, Jenny Townhill, Patricia Trigo Cubillo, Wildson Vieira da Silva, Marleen R van Walsem, Carina Whalstedt, Marie-Noelle Witjes-Ané, Grzegorz Witkowski , Abigail Wright, Daniel Zielonka, Eugeniusz Zielonka, Paola Zinzi

## AUSTRIA

Graz (Medizinische Universitäts Graz, Psychiatrie): Raphael M Bonelli, Sabine Lilek, Karen
Hecht, Brigitte Herranhof, Anna Holl (formerly Hödl), Hans-Peter Kapfhammer, Michael
Koppitz, Markus Magnet, Nicole Müller, Daniela Otti, Annamaria Painold, Karin Reisinger, Monika Scheibl, Helmut Schöggl, Jasmin Ullah

Innsbruck (Universitätsklinik Innsbruck, Neurologie): Eva-Maria Braunwarth, Florian Brugger, Lisa Buratti, Eva-Maria Hametner, Caroline Hepperger, Christiane Holas, Anna Hotter, Anna Hussl, Christoph Müller, Werner Poewe, Klaus Seppi, Fabienne Sprenger, Gregor Wenning

## BELGIUM

Bierbeek: Andrea Boogaerts, Godelinde Calmeyn, Isabelle Delvaux, Dirk Liessens, Nele Somers
Charleroi (Institut de Pathologie et de Génétique (IPG)): Michel Dupuit, Cécile Minet,
Dominique van Paemel, Pascale Ribaï, Christine Verellen-Dumoulin
Leuven: (Universitair Ziekenhuis Gasthuisberg,): Andrea Boogaerts, Wim Vandenberghe, Dimphna van Reijen

## CZECH REPUBLIC

Prague (Extrapyramidové centrum, Neurologická klinika, 1. LF UK a VFN): Jiří Klempíŕ, Veronika Majerová, Jan Roth, Irena Stárková

## DENMARK

Copenhagen (Neurogenetics Clinic, Danish Dementia Research Centre, Rigshospitalet,
University of Copenhagen): Lena E. Hjermind, Oda Jacobsen, Jørgen E Nielsen, Ida Unmack Larsen, Tua Vinther-Jensen

FINLAND
Turku-Suvituuli (Rehabilitation Centre Suvituuli): Heli Hiivola, Hannele Hyppönen, Kirsti Martikainen, Katri Tuuha

FRANCE
Angers (Centre de référence des maladies neurogénétique- CHU d'Angers): Philippe Allain,
Dominique Bonneau, Marie Bost, Bénédicte Gohier, Marie-Anne Guérid, Audrey Olivier,

Adriana Prundean, Clarisse Scherer-Gagou, Christophe Verny
Bordeaux (Hôpital CHU Pellegrin): Blandine Babiloni, Sabrina Debruxelles, Charlotte Duché,
Cyril Goizet, Laetitia Jameau, Danielle Lafoucrière, Umberto Spampinato

## Lille-Amiens:

Lille (CHRU Roger Salengro) : Rekha Barthélémy, Christelle De Bruycker, Maryline Cabaret, Anne-Sophie Carette, Eric Decorte Luc Defebvre, Marie Delliaux, Arnaud Delval, Alain Destee, Kathy Dujardin, Marie-Hélène Lemaire, Sylvie Manouvrier, Mireille Peter, Lucie Plomhouse, Bernard Sablonnière, Clémence Simonin, Stéphanie Thibault-Tanchou, Isabelle Vuillaume

Amiens (CHU Nord) : Marcellin Bellonet, Hassan Berrissoul, Stéphanie Blin, Françoise Courtin, Cécile Duru, Véronique Fasquel, Olivier Godefroy, Pierre Krystkowiak, Béatrice Mantaux, Martine Roussel, Sandrine Wannepain

Marseille (Hôpital La Timone) : Jean-Philippe Azulay, Marie Delfini, Alexandre Eusebio, Frédérique Fluchere, Laura Mundler

Strasbourg (Hôpital Civil) : Mathieu Anheim, Celine Julié, Ouhaid Lagha Boukbiza, Nadine
Longato, Gabrielle Rudolf, Christine Tranchant, Marie-Agathe Zimmermann
GERMANY

Aachen (Universitätsklinikum Aachen, Neurologische Klinik): Christoph Michael Kosinski, Eva Milkereit, Daniela Probst, Kathrin Reetz, Christian Sass, Johannes Schiefer, Christiane Schlangen, Cornelius J. Werner

## Berlin (Klinik und Poliklinik für Neurologie - Charité - Universitätsmedizin Berlin): Harald

Gelderblom, Josef Priller, Harald Prüß, Eike Jakob Spruth
Bochum (Huntington-Zentrum (NRW) Bochum im St. Josef-Hospital): Gisa Ellrichmann, Lennard Herrmann, Rainer Hoffmann, Barbara Kaminski, Peter Kotz, Christian Prehn, Carsten

Saft
Dinslaken (Reha Zentrum in Dinslaken im Gesundheitszentrums Lang): Herwig Lange, Robert Maiwald

Dresden (Universitätsklinikum Carl Gustav Carus an der Technischen Universität
Dresden, Klinik und Poliklinik für Neurologie): Matthias Löhle, Antonia Maass, Simone
Schmidt, Cecile Bosredon, Alexander Storch, Annett Wolz, Martin Wolz
Freiburg (Universitätsklinik Freiburg, Neurologie): Philipp Capetian, Johann Lambeck, Birgit Zucker

Hamburg (Universitätsklinikum Hamburg-Eppendorf, Klinik und Poliklinik für
Neurologie): Kai Boelmans, Christos Ganos, Walburgis Heinicke, Ute Hidding, Jan Lewerenz, Alexander Münchau, Michael Orth, Jenny Schmalfeld, Lars Stubbe, Simone Zittel

Hannover (Neurologische Klinik mit Klinischer Neurophysiologie, Medizinische
Hochschule Hannover): Gabriele Diercks, Dirk Dressler, Heike Gorzolla, Christoph Schrader, Pawel Tacik

Itzehoe (Schwerpunktpraxis Huntington, Neurologie und Psychiatrie): Michael Ribbat Marburg KPP (Klinik für Psychiatrie und Psychotherapie Marburg-Süd): Bernhard Longinus

Marburg Uni (Universität Marburg, Neurologie): Katrin Bürk, Jens Carsten Möller, Ida Rissling

München (Huntington-Ambulanz im Neuro-Kopfzentrum - Klinikum rechts der Isar der Neurologischen Klinik und Poliklinik der Technischen Universität München): Mark Mühlau, Alexander Peinemann, Michael Städtler, Adolf Weindl, Juliane Winkelmann, Cornelia Ziegler

Münster (Universitätsklinikum Münster, Klinik und Poliklinik für Neurologie): Natalie Bechtel, Heike Beckmann, Stefan Bohlen, Eva Hölzner, Herwig Lange, Ralf Reilmann, Stefanie Rohm, Silke Rumpf, Sigrun Schepers, Natalia Weber

Taufkirchen (Isar-Amper-Klinikum - Klinik Taufkirchen (Vils)): Matthias Dose, Gabriele Leythäuser, Ralf Marquard, Tina Raab, Alexandra Wiedemann

Ulm (Universitätsklinikum Ulm, Neurologie): Katrin Barth, Andrea Buck, Julia Connemann, Daniel Ecker, Carolin Geitner, Christine Held, Andrea Kesse, Bernhard Landwehrmeyer, Christina Lang, Jan Lewerenz, Franziska Lezius, Solveig Nepper, Anke Niess, Michael Orth, Ariane Schneider, Daniela Schwenk, Sigurd Süßmuth, Sonja Trautmann, Patrick Weydt

## ITALY

Bari Clinica Neurologica - Neurophysiopatology of Pain Unit UNIVERSITA' DI BARI): Claudia Cormio, Vittorio Sciruicchio, Claudia Serpino, Marina de Tommaso

Bologna (DIBINEM - Alma Mater Studiorum - Università di Bologna; IRCCS Istituto delle Scienze Neurologiche di Bologna): Sabina Capellari, Pietro Cortelli, Roberto Galassi, Rizzo Giovanni, Roberto Poda, Cesa Scaglione

Florence (Dipartimento di Scienze Neurologiche e Psichiatriche Universita' degli Studi di Firenze-Azienda Ospedaliera Universitaria Careggi): Elisabetta Bertini, Elena Ghelli, Andrea Ginestroni, Francesca Massaro, Claudia Mechi, Marco Paganini, Silvia Piacentini, Silvia Pradella, Anna Maria Romoli, Sandro Sorbi

Genoa (Dipartimento di Neuroscienze, Riabilitazione, Oftalmologia, Genetica e Scienze
Materno-Infantili, Università di Genova): Giovanni Abbruzzese, Monica Bandettini di Poggio, Giovanna Ferrandes, Paola Mandich, Roberta Marchese

Milan (Fondazione IRCCS Istituto Neurologico Carlo Besta):

Alberto Albanese, Daniela Di Bella, Anna Castaldo, Stefano Di Donato, Cinzia Gellera, Silvia
Genitrini, Caterina Mariotti, Daniela Monza, Lorenzo Nanetti, Dominga Paridi, Paola Soliveri, Chiara Tomasello

Naples (Dipartimento di Neuroscienze, Scienze Riproduttive e Odontostomatologiche, Università Federico II): Giuseppe De Michele, Luigi Di Maio, Marco Massarelli, Silvio Peluso, Alessandro Roca, Cinzia Valeria Russo, Elena Salvatore, Pierpaolo Sorrentino

Pozzilli (IS) (Centro di Neurogenetica e Malattie Rare - IRCCS Neuromed): Enrico Amico, Mariagrazia Favellato, Annamaria Griguoli, Irene Mazzante, Martina Petrollini, Ferdinando Squitieri and Rome (Lega Italiana Ricerca Huntington e malattie correlate - onlus /
www.LIRH.it): Barbara D'Alessio, Chiara Esposito
Rome (Istituto di Farmacologia Traslazionale \& Istituto di Scienze e Tecnologie della Cognizione /CNR, Istituto di Neurologia Università Cattolica del Sacro Cuore): Anna Rita Bentivoglio, Marina Frontali, Arianna Guidubaldi, Tamara Ialongo, Gioia Jacopini, Carla Piano, Silvia Romano, Francesco Soleti, Maria Spadaro, Paola Zinzi

## NETHERLANDS

Enschede (Medisch Spectrum Twente): Monique S.E. van Hout, Marloes E. Verhoeven, Jeroen P.P. van Vugt, A. Marit de Weert

Groningen (Polikliniek Neurologie): J.J.W. Bolwijn, M. Dekker, B. Kremer, K.L. Leenders, J.C.H. van Oostrom

Leiden (Leiden University Medical Centre (LUMC)): Simon J. A. van den Bogaard, Reineke
Bos, Eve M. Dumas, Ellen P. 't Hart, Raymund A.C. Roos
Nijmegen (Universitair Medisch Centrum St. Radboud, Neurology): Berry Kremer, C.C.P.
Verstappen

## NORWAY

Oslo University Hospital (Rikshospitalet, Dept. of Medical Genetics and Dept. of Neurology): Olaf Aaserud, Jan Frich C., Arvid Heiberg, Marleen R. van Walsem, Ragnhild Wehus

Oslo University Hospital (Ulleval, Dept. of Medical Genetics and Dept.of
Neurorehabilitation): Kathrine Bjørgo, Madeleine Fannemel, Per F. Gørvell, Eirin Lorentzen, Susana Pro Koivisto, Lars Retterstøl, Bodil Stokke

Trondheim (St. Olavs Hospital): Inga Bjørnevoll, Sigrid Botne Sando
POLAND
Gdansk (St. Adalbert Hospital, Gdansk, Medical University of Gdansk, Neurological and
Psychiatric Nursing Dpt.): Artur Dziadkiewicz, Malgorzata Nowak, Piotr Robowski, Emilia Sitek, Jaroslaw Slawek, Witold Soltan, Michal Szinwelski

Katowice (Medical University of Silesia, Katowice): Magdalena Blaszcyk, Magdalena Boczarska-Jedynak, Ewelina Ciach-Wysocka, Agnieszka Gorzkowska, Barbara Jasinska-Myga, Gabriela Kłodowska-Duda, Gregorz Opala, Daniel Stompel

Krakow (Krakowska Akademia Neurologii): Krzysztof Banaszkiewicz, Dorota Boćwińska, Kamila Bojakowska-Jaremek, Małgorzata Dec, Malgorzata Krawczyk, Monika Rudzińska, Elżbieta Szczygie $\underset{,}{ }$ Andrzej Szczudlik, Anna Wasielewska, Magdalena Wójcik

Poznan (Poznan University of Medical Sciences, Poland): Anna Bryl, Anna Ciesielska, Aneta
Klimberg, Jerzy Marcinkowski, Husam Samara, Justyna Sempołowicz, Daniel Zielonka
Warsaw-MU (Medical University of Warsaw, Neurology): Anna Gogol (formerly
Kalbarczyk), Piotr Janik, Hubert Kwiecinski, Zygmunt Jamrozik
Warsaw-IPiN (Institute of Psychiatry and Neurology Dep. of Genetics, First Dep. of

Neurology): Jakub Antczak, Katarzyna Jachinska, Wioletta Krysa, Maryla Rakowicz, Przemyslaw Richter, Rafal Rola, Danuta Ryglewicz, Halina Sienkiewicz-Jarosz, Iwona Stępniak, Anna Sutek, Grzegorz Witkowski, Jacek Zaremba, Elzbieta Zdzienicka, Karolina ZieoraJakutowicz

## PORTUGAL

Coimbra (Hospital Universitário de Coimbra): Cristina Januário, Filipa Júlio
Lisbon (Clinical Pharmacology Unit, Instituto de Medicina Molecular, Faculty of Medicine,
University of Lisbon): Joaquim J Ferreira, Miguel Coelho, Leonor Correia Guedes, Tiago
Mendes, Tiago Mestre, Anabela Valadas
Porto (Hospital de São João, (Faculdade de Medicina da Universidade do Porto)): Carlos Andrade, Miguel Gago, Carolina Garrett, Maria Rosália Guerra.

SPAIN
Badajoz (Hospital Infanta Cristina): Carmen Durán Herrera, Patrocinio Moreno Garcia
Barcelona-Hospital Mútua de Terrassa: Miquel Aguilar Barbera, Dolors Badenes Guia, Laura
Casas Hernanz, Judit López Catena, Pilar Quiléz Ferrer, Ana Rojo Sebastián, Gemma Tome
Carruesco
Barcelona-Bellvitge (Hospital Universitari de Bellvitge): Jordi Bas, Núria Busquets, Matilde Calopa

Barcelona-Merced (Hospital Mare de Deu de La Merced): Misericordia Floriach Robert, Celia Mareca Viladrich, Jesús Miguel Ruiz Idiago, Antonio Villa Riballo

Burgos (Servicio de Neurología Hospital General Yagüe): Esther Cubo, Cecilia Gil Polo,
Natividad Mariscal Perez, Jessica Rivadeneyra
Granada (Hospital Universitario San Cecilio, Neurología): Francisco Barrero, Blas Morales

Madrid-Clinico (Hospital Clínico Universitario San Carlos): María Fenollar, Rocío GarcíaRamos García, Paloma Ortega, Clara Villanueva

Madrid RYC (Hospital Ramón y Cajal, Neurología): Javier Alegre, Mónica Bascuñana, Juan Garcia Caldentey, Marta Fatás Ventura, Guillermo García Ribas, Justo García de Yébenes, José Luis López-Sendón Moreno, Patricia Trigo Cubillo

Madrid FJD (Madrid-Fundación Jiménez Díaz): Javier Alegre, Fernando Alonso Frech, Justo García de Yébenes, Pedro J García Ruíz, Asunción Martínez-Descals, Rosa Guerrero, María José Saiz Artiga, Vicenta Sánchez

Murcia (Hospital Universitario Virgen de la Arrixaca): María Fuensanta Noguera Perea, Lorenza Fortuna, Salvadora Manzanares, Gema Reinante, María Martirio Antequera Torres, Laura Vivancos Moreau

Oviedo (Hospital Central de Asturias): Sonia González González, Luis Menéndez Guisasola, Carlos Salvador, Esther Suaréz San Martín

Palma de Mallorca (Hospital Universitario Son Espases): Inés Legarda Ramirez, Aranzazú Gorospe, Mónica Rodriguez Lopera, Penelope Navas Arques, María José Torres Rodríguez, Barbara Vives Pastor

Pamplona (Complejo Hospitalario de Navarra): Itziar Gaston, Maria Dolores MartinezJaurrieta, Maria A. Ramos-Arroyo

Sevilla ("Hospital Virgen Macarena"): Jose Manuel Garcia Moreno, Carolina Mendez Lucena, Fatima Damas Hermoso, Eva Pacheco Cortegana, José Chacón Peña, Luis Redondo

Sevilla (Hospital Universitario Virgen del Rocío): Fátima Carrillo, María Teresa Cáceres, Pablo Mir, María José Lama Suarez, Laura Vargas-González

Valencia (Hospital la Fe): Maria E. Bosca, Francisco Castera Brugada, Juan Andres Burguera,

Anabel Campos Garcia, Carmen Peiró Vilaplana

## SWEDEN

Göteborg (Sahlgrenska University Hospital): Peter Berglund, Radu Constantinescu, Gunnel Fredlund, Ulrika Høsterey-Ugander, Petra Linnsand, Liselotte Neleborn-Lingefjärd, Jan

Wahlström, Magnus Wentzel
Umeå (Umeå University Hospital): Ghada Loutfi, Carina Olofsson, Eva-Lena Stattin, Laila
Westman, Birgitta Wikström

## SWITZERLAND

Bern: Jean-Marc Burgunder, Yanik Stebler (Swiss HD Zentrum), Alain Kaelin, Irene Romero, Michael Schüpbach, Sabine Weber Zaugg (Zentrum für Bewegungsstörungen, Neurologische Klinik und Poliklinik, Universität Bern)

Zürich (Department of Neurology, University Hospital Zürich): Maria Hauer, Roman
Gonzenbach, Hans H. Jung, Violeta Mihaylova, Jens Petersen

## UNITED KINGDOM

Aberdeen (NHS Grampian Clinical Genetics Centre \& University of Aberdeen): Roisin
Jack, Kirsty Matheson, Zosia Miedzybrodzka, Daniela Rae, Sheila A Simpson, Fiona Summers, Alexandra Ure, Vivien Vaughan

Birmingham (The Barberry Centre, Dept of Psychiatry): Shahbana Akhtar, Jenny Crooks, Adrienne Curtis, Jenny de Souza (Keylock), John Piedad, Hugh Rickards, Jan Wright

Bristol (North Bristol NHS Trust, Southmead hospital): Elizabeth Coulthard, Louise Gethin, Beverley Hayward, Kasia Sieradzan, Abigail Wright

Cambridge (Cambridge Centre for Brain Repair, Forvie Site): Matthew Armstrong,
Roger A. Barker, Deidre O’Keefe, Anna Di Pietro, Kate Fisher, Anna Goodman, Susan Hill,

Ann Kershaw, Sarah Mason, Nicole Paterson, Lucy Raymond, Rachel Swain, Natalie Valle Guzman

Cardiff (Schools of Medicine and Biosciences, Cardiff University): Monica Busse, Cynthia Butcher, Jenny Callaghan, Stephen Dunnett, Catherine Clenaghan, Ruth Fullam, Olivia Handley, Sarah Hunt, Lesley Jones, Una Jones, Hanan Khalil, Sara Minster, Michael Owen, Kathleen Price, Anne Rosser, Jenny Townhill

Edinburgh (Molecular Medicine Centre, Western General Hospital, Department of Clinical
Genetics): Maureen Edwards, Carrie Ho (Scottish Huntington's Association), Teresa Hughes (Scottish Huntington's Association), Marie McGill, Pauline Pearson, Mary Porteous, Paul Smith (Scottish Huntington's Association)

Fife (Scottish Huntington's Association Whyteman's Brae Hospital): Peter Brockie, Jillian Foster, Nicola Johns, Sue McKenzie, Jean Rothery, Gareth Thomas, Shona Yates

Gloucester (Department of Neurology Gloucestershire Royal Hospital): Liz Burrows, Carol Chu, Amy Fletcher, Deena Gallantrae, Stephanie Hamer, Alison Harding, Stefan Klöppel, Alison Kraus, Fiona Laver, Monica Lewis, Mandy Longthorpe, Ivana Markova, Ashok Raman, Nicola Robertson, Mark Silva, Aileen Thomson, Sue Wild, Pam Yardumian

Hull (Castle Hill Hospital): Carol Chu, Carole Evans, Deena Gallentrae, Stephanie Hamer, Alison Kraus, Ivana Markova, Ashok Raman

Leeds (Chapel Allerton Hospital, Department of Clinical Genetics): Leeds (Chapel Allerton
Hospital, Clinical Genetics): Carol Chu, Stephanie Hamer, Emma Hobson, Stuart Jamieson, Alison Kraus, Ivana Markova, Ashok Raman, Hannah Musgrave, Liz Rowett, Jean Toscano, Sue Wild, Pam Yardumian

Leicester (Leicestershire Partnership Trust, Mill Lodge): Colin Bourne, Jackie Clapton,

Carole Clayton, Heather Dipple, Dawn Freire-Patino, Janet Grant, Diana Gross, Caroline Hallam, Julia Middleton, Ann Murch, Catherine Thompson

Liverpool (Walton Centre for Neurology and Neurosurgery): Sundus Alusi, Rhys Davies, Kevin Foy, Emily Gerrans, Louise Pate

London (Guy's Hospital): Thomasin Andrews, Andrew Dougherty, Charlotte Golding, Fred Kavalier, Hana Laing, Alison Lashwood, Dene Robertson, Deborah Ruddy, Alastair Santhouse, Anna Whaite

London (The National Hospital for Neurology and Neurosurgery): Thomasin Andrews, Stefania Bruno, Karen Doherty, Charlotte Golding, Salman Haider, Davina Hensman, Nayana Lahiri, Monica Lewis, Marianne Novak, Aakta Patel, Nicola Robertson, Elisabeth Rosser, Sarah Tabrizi, Rachel Taylor, Thomas Warner, Edward Wild

Manchester (Genetic Medicine, University of Manchester, Manchester Academic Health Sciences Centre and Central Manchester University Hospitals NHS Foundation Trust):

Natalie Arran, Judith Bek, Jenny Callaghan, David Craufurd, Ruth Fullam, Marianne Hare, Liz Howard, Susan Huson, Liz Johnson, Mary Jones, Helen Murphy, Emma Oughton, Lucy Partington-Jones, Dawn Rogers, Andrea Sollom, Julie Snowden, Cheryl Stopford, Jennifer Thompson, Iris Trender-Gerhard, Nichola Verstraelen (formerly Ritchie), Leann Westmoreland

Oxford (Oxford University Hospitals NHS Trust, Dept. of Neurosciences, University of Oxford): Richard Armstrong, Kathryn Dixon, Andrea H Nemeth, Gill Siuda, Ruth Valentine Plymouth (Plymouth Huntington Disease Service, Mount Gould Hospital): David Harrison, Max Hughes, Andrew Parkinson, Beverley Soltysiak

Sheffield (The Royal Hallamshire Hospital- Sheffield Children's Hospital): Oliver
Bandmann, Alyson Bradbury, Paul Gill, Helen Fairtlough, Kay Fillingham, Isabella Foustanos,

Mbombe Kazoka, Kirsty O'Donovan, Nadia Peppa, Cat Taylor, Katherine Tidswell, Oliver Quarrell

EHDN's associate site in Singapore: National Neuroscience Institute Singapore: Jean-Marc
Burgunder, Puay Ngoh Lau, Emmanul Pica, Louis Tan

Table S1. Genotype of replication samples.

| fluidigm. 1 | 0.4320 | C C | C T | C T | A A | A G | A G | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm. 2 | 3.3616 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm. 3 | -9.7580 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 4 | 16.2420 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm. 5 | 1.6159 | C C | C T | T T | A G | A G | A G | G G |
| fluidigm. 6 | 10.1557 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 7 | 2.2804 | C C | C T | T T | A A | A G | A A | C G |
| fluidigm. 8 | 14.0958 | C C | C T | C T | A A | G G | A A | G G |
| fluidigm. 9 | 16.3177 | C C | T T | T T | A G | G G | A A | G G |
| fluidigm. 10 | -10.6384 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm. 11 | 0.0847 | C T | T T | T T | A A | G G | A G | G G |
| fluidigm. 12 | 2.6159 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 13 | 5.0847 | C C | C T | T T | A G | A G | A A | C G |
| fluidigm. 14 | 0.6159 | C C | T T | T T | A A | A A | A A | G G |
| fluidigm. 15 | 7.2804 | C C | T T | T T | A A | G G | A G | G G |
| fluidigm. 16 | -6.6823 | C C | C T | C T | A A | A G | A A | G G |
| fluidigm. 17 | 1.8897 | C C | C C | T T | A G | G G | A A | G G |
| fluidigm. 18 | 1.3616 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm. 19 | -0.7196 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm. 20 | 5.8345 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 21 | 4.1885 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm. 22 | -7.8115 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 23 | 6.4320 | C C | T T | T T | A G | A G | A G | C G |
| fluidigm. 24 | -3.3841 | C C | C T | T T | A A | A G | A A | C G |
| fluidigm. 25 | 6.2420 | C C | T T | T T | A A | A G | A G | G G |
| fluidigm. 26 | 6.2420 | C T | T T | T T | A A | A A | A A | G G |
| fluidigm. 27 | -1.6384 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 28 | -0.3841 | C C | T T | T T | A A | A A | A A | G G |
| fluidigm. 29 | 14.2804 | C C | C T | C T | A A | G G | A A | G G |
| fluidigm. 30 | -3.1103 | C C | T T | T T | A G | G G | A A | G G |
| fluidigm. 31 | 11.2420 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 32 | 12.3177 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 33 | -21.6823 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 34 | -16.1103 | C C | T T | T T | A G | A G | A G | G G |
| fluidigm. 35 | -2.5680 | C C | C T | C T | A A | A A | A A | G G |
| fluidigm. 36 | -5.6823 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 37 | 8.8897 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 38 | -2.0313 | C C | C T | C T | A G | A A | A A | G G |
| fluidigm. 39 | -4.9042 | C C | T T | T T | G G | G G | A G | C G |
| fluidigm. 40 | -6.1103 | C C | C C | T T | A G | G G | A A | G |


| fluidigm. 41 | -3.6823 | C C | C T | T T | A G | A A | A A | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm. 42 | 9.3177 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm. 43 | 14.3177 | C T | C C | C T | A A | A G | A G | G G |
| fluidigm. 44 | 6.1557 | C C | C T | T T | G G | A G | A A | G G |
| fluidigm. 45 | 5.8897 | C C | T T | T T | A A | A G | A G | G G |
| fluidigm. 46 | -7.7580 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm. 47 | 4.8897 | C C | C T | T T | A G | G G | A G | G G |
| fluidigm. 48 | -5.1103 | C C | C C | T T | A G | A G | A A | G G |
| fluidigm. 49 | 4.0958 | C T | C C | C T | A A | G G | A A | G G |
| fluidigm. 50 | -8.6384 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 51 | -5.6384 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm. 52 | -2.7196 | C C | T T | C T | A A | A G | A A | G G |
| fluidigm. 53 | -13.7580 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm. 54 | 6.8897 | C C | T T | T T | A G | G G | A A | G G |
| fluidigm. 55 | -3.7196 | C C | C C | T T | A A | A G | A G | G G |
| fluidigm. 56 | -1.6823 | C C | C T | T T | A G | A A | A A | G G |
| fluidigm. 57 | 7.4671 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm. 58 | 7.3177 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 59 | 2.2420 | C T | C T | T T | A A | A G | A A | G G |
| fluidigm. 60 | -1.7196 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 61 | -7.7580 | C C | T T | T T | A A | A G | A A | C G |
| fluidigm. 62 | -7.7196 | C T | C T | T T | A G | A G | A A | G G |
| fluidigm. 63 | -1.9153 | C C | T T | T T | A A | A G | A G | G G |
| fluidigm. 64 | 1.4671 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 65 | -0.5680 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm. 66 | -4.7580 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 67 | 1.2804 | C C | T T | T T | A G | G G | A A | G G |
| fluidigm. 68 | 0.2804 | C C | C C | T T | A A | A A | A A | G G |
| fluidigm. 69 | -4.1103 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 70 | 1.2420 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 71 | 6.4320 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 72 | 0.3616 | C C | C T | T T | G G | A G | A A | G G |
| fluidigm. 73 | -1.9153 | C C | T T | T T | A A | A A | A A | G G |
| fluidigm. 74 | -8.5680 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm. 75 | 5.2420 | C C | T T | T T | A G | G G | A G | G G |
| fluidigm. 76 | 2.8897 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm. 77 | 2.4320 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 78 | -2.7580 | C C | C T | C T | A G | A G | A A | G G |
| fluidigm. 79 | 0.8897 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm. 80 | -1.5680 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm. 81 | -2.3841 | C C | C T | T T | A A | G G | A A | C G |
| fluidigm. 82 | 3.2420 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 83 | 4.0847 | C C | T T | T T | A A | A G | A A | G G |


| fluidigm. 84 | 6.0958 | C C | C T | T T | A G | A G | A A | C G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm. 85 | 2.3177 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm. 86 | 1.3177 | C T | C T | T T | A A | A A | A A | G G |
| fluidigm. 87 | 6.4320 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm. 88 | 3.0958 | C T | C T | T T | A A | G G | A A | G G |
| fluidigm. 89 | -7.6823 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 90 | 0.0958 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 91 | -3.7580 | C C | C T | T T | G G | G G | A G | G G |
| fluidigm. 92 | 6.0958 | C T | T T | T T | A G | A G | A A | G G |
| fluidigm. 93 | -17.7580 | C C | C C | T T | G G | G G | A A | G G |
| fluidigm. 94 | -2.5680 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 95 | 1.4320 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 96 | 22.0958 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 97 | -4.5680 | C C | C T | 00 | A G | A A | A A | G G |
| fluidigm. 98 | -0.6823 | C C | C T | T T | A A | G G | A A | C G |
| fluidigm. 99 | 4.4320 | C C | C C | T T | A A | A G | A G | G G |
| fluidigm.10( | 0.8897 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.101 | 3.0958 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm. $10-$ | 9.8897 | C C | C C | T T | A G | A G | A A | G G |
| fluidigm.10: | -12.1103 | C C | C T | T T | A G | G G | A G | G G |
| fluidigm. 10 | -5.5680 | C C | C T | T T | G G | A G | A A | C G |
| fluidigm.10: | 7.2420 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 10 t | -19.6823 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm.10: | -11.1103 | C C | C T | T T | A G | G G | A G | G G |
| fluidigm. 10 ¢ | 3.8897 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.10s | 11.6159 | C C | C C | T T | A G | G G | A G | G G |
| fluidigm.11( | -14.9042 | C C | C T | 00 | A G | A A | A A | G G |
| fluidigm. 111 | -7.6384 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.112 | -6.7580 | C C | T T | 00 | A A | G G | A A | G G |
| fluidigm.11ः | 0.2420 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. $11<$ | 1.2804 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm.11: | 7.2420 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.11t | -0.1103 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm.11; | -8.7580 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.118 | 2.0958 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.11s | 21.3177 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 121 | -9.7580 | C T | C C | T T | A A | A G | A A | G G |
| fluidigm. 121 | -0.3841 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm.12\% | 5.2420 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm.12: | 8.2804 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm. 12 | -7.1103 | C C | C T | 00 | A A | A A | A A | G G |
| fluidigm.12: | -0.7196 | C C | T T | T T | A A | A G | A G | G G |
| fluidigm.12t | -0.5680 | C C | T T | T T | G G | A G | A A | G G |


| fluidigm.12; | -5.1103 | C C | C T | T T | A A | A G | A A | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm. 12 ¢ | -10.9042 | C C | T T | 00 | A A | A A | A A | G G |
| fluidigm.12 ${ }^{\text {S }}$ | -9.9042 | C C | C T | T T | A G | A A | A A | C G |
| fluidigm.13( | -0.0313 | C C | C T | 00 | A A | G G | A A | G G |
| fluidigm. 131 | -6.6823 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.132 | -4.1103 | C C | C C | T T | A G | A G | A A | C G |
| fluidigm.13: | -3.6823 | C C | C T | 00 | A G | A G | A A | G G |
| fluidigm. 13 | -21.1103 | C C | T T | T T | A G | G G | A A | C G |
| fluidigm.13: | 2.2420 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.13t | -6.9042 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.13: | -10.6823 | C T | C T | T T | A A | A G | A G | C G |
| fluidigm.138 | -1.3841 | C C | T T | T T | A G | G G | A A | C G |
| fluidigm.13s | 5.4320 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.14( | 1.9687 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm.141 | 4.8897 | C C | T T | T T | A A | A A | A A | C G |
| fluidigm.14^2 | -6.5680 | C C | C T | T T | A G | A A | A A | G G |
| fluidigm.14: | -14.1103 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.14 | -12.6823 | C C | C T | T T | G G | A G | A A | G G |
| fluidigm.14ः | -2.9042 | C C | C C | T T | A G | G G | A A | G G |
| fluidigm.14t | 4.3177 | C C | T T | T T | A A | G G | A G | G G |
| fluidigm.14; | -0.7580 | C C | C T | T T | A G | A A | A A | G G |
| fluidigm.14乏 | -2.5680 | C C | C C | T T | A A | A A | A A | G G |
| fluidigm.14¢ | -10.7580 | C C | C T | T T | A A | A G | A A | C G |
| fluidigm.15( | 4.4320 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.151 | -2.9042 | C C | T T | T T | G G | G G | A A | G G |
| fluidigm. 152 | -3.9153 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.15: | 9.8897 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm. 15 | 0.0847 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.15: | -18.9042 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm. $15 t$ | -0.6384 | C C | T T | T T | A A | A A | A A | G G |
| fluidigm. 15 ; | 2.1885 | C C | T T | T T | A G | A A | A A | G G |
| fluidigm. 158 | -9.9042 | C C | C T | C T | A G | A G | A A | G G |
| fluidigm.15s | 1.3177 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.160 | -14.7580 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.161 | -2.7196 | C C | T T | T T | A G | G G | A A | G G |
| fluidigm.16: | 1.8897 | C C | C C | C T | A A | A G | A G | G G |
| fluidigm.16: | 3.2420 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 162 | -4.0313 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm.16: | -6.3841 | C C | C T | T T | A A | G G | A G | G G |
| fluidigm.16t | -8.9042 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm.16; | 1.4671 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.168 | -3.7196 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm.16s | 2.8897 | C C | C T | T T | A A | G G | A A | G G |


| fluidigm.17( | -17.5680 | C C | C T | T T | A G | G G | A A | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm. 171 | -5.9042 | C C | T T | T T | A A | A A | A A | G G |
| fluidigm. 172 | -0.7196 | C C | C C | T T | A G | A A | A A | G G |
| fluidigm.17: | 6.2420 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm. $17<$ | -12.9042 | C C | C T | T T | A A | G G | A G | G G |
| fluidigm.17? | 0.8897 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 17 t | 14.6159 | C T | T T | T T | A A | G G | A A | G G |
| fluidigm.17\% | -1.0313 | C C | C T | T T | A A | G G | A G | G G |
| fluidigm. 178 | -8.1103 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm.17s | 12.0958 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 181 | -5.7580 | C C | T T | T T | A G | G G | A A | G G |
| fluidigm. 181 | 2.2420 | C T | C T | T T | A A | G G | A A | G G |
| fluidigm.18* | -4.6823 | C C | C T | T T | A G | A A | A A | G G |
| fluidigm.18: | -6.5680 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.18< | 0.0847 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.18: | -2.7196 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 186 | 3.9687 | C C | C C | T T | A A | G G | A G | G G |
| fluidigm.18: | -4.1103 | C C | C T | T T | A A | A A | A G | G G |
| fluidigm.18\& | 7.0958 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.18s | 8.2420 | C C | T T | T T | A G | G G | A A | G G |
| fluidigm.19( | 8.2804 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.19] | -1.7196 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.192 | -6.6823 | C C | C T | T T | A G | A G | A G | G G |
| fluidigm.19: | 10.4320 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.19 | 1.3616 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm.19: | -7.5680 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.19t | -5.7196 | C C | C T | C T | A A | A G | A A | G G |
| fluidigm.19; | 2.2804 | C C | C T | T T | A A | G G | 00 | G G |
| fluidigm.198 | -1.6384 | C C | C T | T T | A A | A G | A A | C G |
| fluidigm.19s | 0.4320 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 200 | 2.8897 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm.20] | 15.2804 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 20 - | 0.8897 | C T | T T | T T | A G | A G | A G | G G |
| fluidigm.20: | -2.7580 | C T | T T | T T | A A | G G | A A | G G |
| fluidigm. 20 | 2.1557 | C C | C T | T T | A A | A G | A A | C G |
| fluidigm.20: | -2.6823 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm. 20 ( | -2.5680 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm.20; | 11.8897 | C C | T T | T T | A G | A A | A G | G G |
| fluidigm. 20 \& | -0.6384 | C C | C T | T T | A G | G G | A A | 00 |
| fluidigm. $20 \leq$ | 9.3177 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm.21( | 14.8897 | C T | T T | T T | A G | 00 | A G | G G |
| fluidigm. 211 | 4.1557 | C C | T T | T T | A A | A G | 00 | G G |
| fluidigm. 212 | 4.8897 | C C | T T | T T | A A | A G | A A | G G |


| fluidigm.21ः | -1.1103 | C T | C T | T T | A A | G G | A A | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm. $21<$ | -1.6384 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 21 : | -8.1103 | C T | C T | T T | A A | A G | A A | G G |
| fluidigm. 21 t | 1.2420 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 21 , | 6.0958 | C C | C C | T T | A G | G G | A A | G G |
| fluidigm. 218 | 9.8345 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm.21s | -9.7580 | C C | T T | T T | A A | A G | A G | G G |
| fluidigm. 221 | 8.2804 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.221 | -8.6384 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.22\% | 5.8897 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm.22: | 4.8897 | C C | C C | T T | G G | G G | A A | G G |
| fluidigm.22 | -0.7580 | C C | C C | T T | A G | G G | A G | G G |
| fluidigm.22: | 7.3177 | C T | C T | C T | A G | A G | A A | G G |
| fluidigm. 226 | -14.1103 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.22; | -0.1103 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm. 22 \& | -1.9153 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.22s | -3.5680 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 231 | 3.2420 | C T | C T | T T | A A | A G | A A | C G |
| fluidigm. 231 | 9.3177 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm.232- | -1.5680 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.23: | -15.9042 | C C | C T | T T | A G | A G | A G | G G |
| fluidigm. $23<$ | 4.2804 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm.23: | 4.2804 | C C | C C | C T | A A | A A | A A | G G |
| fluidigm. 23 t | 5.3177 | C C | C C | T T | A G | G G | A A | G G |
| fluidigm.23: | -2.6384 | C C | C C | T T | A G | G G | A A | C G |
| fluidigm. 238 | 6.0847 | C C | T T | T T | A A | G G | A G | G G |
| fluidigm.23s | 3.0847 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm.24( | 0.2804 | C T | C T | T T | A A | A G | A A | C G |
| fluidigm. 241 | -14.7580 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm. 24 - | -2.7196 | C C | C T | T T | A G | G G | A G | G G |
| fluidigm.24: | 2.1557 | C C | T T | T T | A G | G G | A A | G G |
| fluidigm. 24 | 13.2420 | C C | C T | T T | A G | A A | A A | C G |
| fluidigm. 24 ! | -28.9042 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm. 24 ¢ | 6.2420 | C T | C T | T T | A A | A G | A G | G G |
| fluidigm.24; | 5.1885 | C C | C T | C T | A G | A A | A A | G G |
| fluidigm. 248 | 3.2804 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.24¢ | 3.8897 | C C | T T | T T | A G | A G | A G | G G |
| fluidigm. 25 ( | -1.9153 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 251 | -1.6823 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm. $25^{\circ}$ | 2.2804 | C C | T T | T T | A A | A A | A A | G G |
| fluidigm. 25 : | 3.2420 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 25 | -8.6384 | C T | C C | T T | A A | A G | A G | G G |
| fluidigm. 25 : | 0.4320 | C C | C T | T T | A A | G G | A A | G G |


| fluidigm. $25 t$ | -24.1103 | C C | C T | T T | A A | A G | A A | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm. 25 , | -19.9042 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm. 258 | -8.9153 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm.25s | -4.7580 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm. 260 | 0.2420 | C C | T T | T T | A G | G G | A A | C G |
| fluidigm. 261 | -0.6384 | C C | C T | T T | A A | G G | A G | G G |
| fluidigm. 26 \% | 0.0958 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.26: | 3.8897 | C C | T T | C T | A A | G G | A G | G G |
| fluidigm. $26<$ | -10.1103 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.26: | 10.4320 | C C | C C | T T | A G | A G | A A | G G |
| fluidigm. $26 t$ | 4.2804 | C C | T T | T T | A A | A G | A A | C G |
| fluidigm.26; | -8.9042 | C C | C C | T T | A A | A A | A A | G G |
| fluidigm. 268 | 2.2804 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.26s | 12.0958 | C C | T T | T T | A A | G G | A A | C G |
| fluidigm.27( | -3.3841 | C C | C T | T T | A G | A G | A A | C G |
| fluidigm. 271 | -1.7580 | C C | T T | T T | A A | A A | A A | G G |
| fluidigm. $27 \%$ | 8.3177 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.27: | 1.8897 | C C | C T | T T | A G | A A | A G | G G |
| fluidigm. $27<$ | -0.1103 | C C | C T | T T | A A | G G | A G | G G |
| fluidigm.27: | 2.3177 | C C | C T | T T | A A | A G | A A | C G |
| fluidigm. $27 t$ | 0.3616 | C C | T T | T T | A G | A G | A G | G G |
| fluidigm.27\% | 6.4320 | C T | C T | T T | A G | G G | A A | G G |
| fluidigm. 278 | 11.0958 | C C | T T | T T | A A | A G | A G | G G |
| fluidigm.27s | 4.8897 | C C | C T | T T | A A | A G | A A | C G |
| fluidigm. 281 | 0.3177 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm. 281 | -2.7580 | C C | T T | C T | A G | G G | A A | G G |
| fluidigm. 28 - | 1.8897 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.28: | -8.1103 | C C | C C | T T | A G | A G | A G | G G |
| fluidigm. 28 | 11.3616 | C C | T T | T T | A G | A A | A A | C G |
| fluidigm.28: | 1.2804 | C T | C T | C T | A G | A G | A A | G G |
| fluidigm. 28 ¢ | -1.7580 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 28 ; | 6.9687 | C C | C C | T T | A G | G G | A A | G G |
| fluidigm. 288 | 5.9687 | C C | C C | T T | A A | G G | A G | G G |
| fluidigm.28s | 4.4320 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm. 29 ( | 3.3177 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.29] | -2.7196 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm.29- | -6.1103 | C C | C T | T T | A G | A G | A G | G G |
| fluidigm.29: | -0.7580 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm.29< | -1.5680 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm.29: | -8.6823 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 29 ¢ | 3.2420 | C C | T T | T T | A A | A A | A A | G G |
| fluidigm.29; | -1.9153 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 29 ¢ | 2.1885 | C C | T T | T T | A G | A A | A A | G G |


| fluidigm.29s | 0.3177 | C C | C C | T T | A A | A A | A A | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm. 300 | -2.6823 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm. 301 | 3.2420 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm. $30 \sim$ | -9.1103 | C C | C C | T T | A A | A A | A A | G G |
| fluidigm.30: | 4.3177 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm. 30 | 0.2804 | C C | T T | T T | A A | G G | 00 | G G |
| fluidigm. 30؛ | 5.4320 | C C | 00 | T T | A A | G G | 00 | G G |
| fluidigm. 300 | 0.0781 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.30\% | 1.8897 | C C | C C | T T | G G | A A | A A | G G |
| fluidigm. 30 \& | -6.1103 | C C | C C | T T | A A | A G | A G | G G |
| fluidigm.30s | 10.4320 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm.31( | -2.9153 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm. 311 | 13.3177 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.312 | 1.4320 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.31: | 4.4320 | C T | C T | T T | A A | A G | A A | G G |
| fluidigm. $31<$ | 12.0958 | C C | T T | T T | A G | G G | A A | G G |
| fluidigm. 31: | 2.8897 | C C | T T | T T | A G | A A | A A | G G |
| fluidigm. 31 t | 1.0847 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.31\% | -6.7580 | C C | C T | T T | A A | A A | A G | G G |
| fluidigm. 318 | -24.1103 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm.31s | -3.6823 | C C | C C | T T | A G | A G | A A | C G |
| fluidigm. 321 | 1.9847 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm.321 | 3.2420 | C C | T T | T T | A G | A A | A A | G G |
| fluidigm.32\% | -18.9153 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.32: | 3.2420 | C C | T T | T T | A G | G G | A A | C G |
| fluidigm.32 | -0.7580 | C T | C T | T T | A A | G G | A G | G G |
| fluidigm. 32 : | 0.3177 | C C | C T | T T | A A | G G | G G | C G |
| fluidigm. 326 | -2.7580 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.32; | 4.0781 | C C | T T | T T | A G | A G | G G | G G |
| fluidigm. 32 \& | -2.7196 | C C | C C | T T | A G | A A | A A | G G |
| fluidigm.32 | -11.5680 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm.33( | 6.2804 | C C | C C | T T | A G | A A | A G | G G |
| fluidigm. 331 | 8.3177 | C C | T T | T T | A A | G G | A G | G G |
| fluidigm.332- | 6.8897 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.33: | -1.7580 | C C | C T | C T | A A | A G | A A | G G |
| fluidigm. 33 | -0.9153 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.33: | -2.7196 | C C | T T | C T | A A | A G | G G | G G |
| fluidigm. $33 t$ | -3.6823 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.33: | 10.3177 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm. 338 | -17.6823 | C C | C T | T T | A A | A G | A A | C G |
| fluidigm.33s | 3.6159 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.34( | 1.2804 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm.34] | -4.6823 | C C | C C | T T | A G | A A | A A | G G |


| fluidigm.342 | 6.4320 | C C | T T | T T | A A | A G | A A | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm.34: | 0.3616 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 34 | 1.2420 | C T | C T | T T | A A | G G | A G | G G |
| fluidigm. 34 ! | 11.3616 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 344 | -6.7580 | C T | C T | T T | G G | A A | A A | G G |
| fluidigm.34; | -5.7580 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 348 | -1.0313 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.34¢ | 2.3177 | C C | T T | T T | A G | G G | A A | G G |
| fluidigm. 351 | 9.6159 | C C | C T | T T | A G | A A | A A | G G |
| fluidigm. 351 | -2.9153 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm. $35{ }^{\circ}$ | -4.7580 | C T | T T | C T | A A | A A | A A | G G |
| fluidigm.35: | -1.6823 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 35 | -2.9153 | C C | C T | T T | A G | G G | A G | G G |
| fluidigm. 35 : | 17.0847 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 35 t | 5.6159 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 35 ; | 1.0958 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 358 | 1.3177 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm.35s | -6.7580 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.360 | 2.4320 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm.361 | -7.6384 | C C | C T | T T | A A | A G | A A | C G |
| fluidigm.362 | 0.8897 | C C | C C | T T | A A | A A | A A | C G |
| fluidigm.36: | 7.8897 | C T | T T | T T | A G | A G | A A | G G |
| fluidigm. 36 | 0.2420 | C C | 00 | T T | A A | A G | 00 | G G |
| fluidigm. 36 \% | -10.9042 | C C | C T | T T | A A | G G | 00 | G G |
| fluidigm.36t | 1.3616 | C C | T T | T T | A A | A A | G G | G G |
| fluidigm.36: | 13.2804 | C C | C C | T T | G G | A G | A A | C G |
| fluidigm. 368 | -13.7196 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm.36s | -0.5680 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.37( | 12.2420 | C T | T T | 00 | A A | A A | A G | G G |
| fluidigm. 371 | 12.3177 | C C | C T | T T | A G | 00 | A G | G G |
| fluidigm.37\% | -7.6823 | C C | T T | T T | A A | A G | A G | G G |
| fluidigm. 37 : | 7.4320 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. $37<$ | 13.2804 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm. 37: | 4.8897 | C C | T T | T T | A A | A G | A G | G G |
| fluidigm. $37 t$ | 0.4320 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm. $37 \%$ | 2.8897 | C C | C T | T T | A A | G G | A A | C G |
| fluidigm. 378 | -3.7196 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm.37s | -11.5680 | C T | C T | T T | A A | A G | A A | G G |
| fluidigm. 381 | -5.9042 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm. 381 | 0.4320 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.38- | -8.1103 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.38: | 3.3616 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm.38 | 8.9687 | C C | C T | T T | A A | A A | A A | G G |


| fluidigm.38: | -5.6384 | C T | C T | T T | A G | A G | A A | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm. 38 t | 8.6159 | C C | T T | T T | A A | A A | A A | G G |
| fluidigm. 38 : | -6.7196 | C C | C C | C T | A A | G G | A G | G G |
| fluidigm. 388 | -5.0313 | C C | T T | C T | A A | A G | A A | G G |
| fluidigm.38¢ | -8.5680 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 390 | -1.7196 | C C | C T | T T | A A | G G | A A | C G |
| fluidigm.39] | 8.2420 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.39- | -1.1103 | C T | T T | T T | A G | A G | A A | G G |
| fluidigm.39: | 1.8897 | C T | C T | T T | A A | A A | A A | C G |
| fluidigm. 39 | 5.0958 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm.39: | 6.3177 | C C | T T | C T | A G | G G | A A | C G |
| fluidigm. 39 t | 8.3177 | C C | C T | C T | A G | A G | A A | G G |
| fluidigm.39; | -14.0313 | C C | C C | C T | A A | A G | A A | G G |
| fluidigm. 39 ¢ | 7.3616 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm.39s | -8.7196 | C C | C T | T T | A G | G G | A G | G G |
| fluidigm.40( | 8.6159 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm.40] | -19.5680 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.40- | 8.3177 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm.40: | 2.6159 | C C | C T | C T | A A | A A | A A | G G |
| fluidigm. 40 - | -5.0313 | C C | C C | T T | A G | G G | A A | G G |
| fluidigm.40: | -1.7196 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 40 ¢ | 0.4320 | C C | T T | T T | A G | A G | A G | G G |
| fluidigm.40: | -3.0313 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm.40\& | -6.7580 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.40s | -5.3841 | C C | C T | T T | A A | G G | A G | G G |
| fluidigm. 411 | -5.1103 | C C | T T | T T | G G | G G | A A | G G |
| fluidigm. 411 | 14.0847 | C C | C C | T T | A G | G G | A A | G G |
| fluidigm.412 | 4.3177 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.41: | 5.0958 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. $41<$ | 4.2420 | C C | C T | T T | A A | A A | A G | G G |
| fluidigm.41: | 0.6159 | C C | C T | T T | A G | A G | A G | G G |
| fluidigm. 41 ¢ | 8.1557 | C C | T T | T T | A A | A A | A A | G G |
| fluidigm.41: | -18.5680 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm. 418 | 3.2420 | C C | C T | T T | G G | A G | A A | G G |
| fluidigm.41s | 4.3616 | C T | C T | T T | A A | A G | A A | G G |
| fluidigm. $42($ | 6.0781 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm. 421 | 5.3616 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. $42 \%$ | 3.2804 | C C | T T | C T | A A | A G | A A | G G |
| fluidigm.42: | 4.6159 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 42 | 9.3616 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm. 42 : | -12.7196 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm. 42 ¢ | 2.2420 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm. 42 ; | 1.1557 | C T | C T | T T | A G | A G | A G | G G |


| fluidigm. 471 | 4.1557 | C C | C T | T T | A A | A G | A A | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm. 472 | 17.3177 | C C | T T | T T | A A | G G | A G | G G |
| fluidigm. 47 : | 10.3177 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. $47<$ | 0.2804 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm. 47 ? | -4.6384 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm. 47 t | -14.7196 | C C | T T | T T | A A | A A | A A | G G |
| fluidigm. $47{ }^{\text {\% }}$ | -3.3841 | C C | C T | T T | A G | A G | A G | G G |
| fluidigm. 478 | 3.8897 | C T | T T | T T | A A | A G | A A | G G |
| fluidigm.47s | -10.7580 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm. 481 | 4.8897 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 481 | -2.1103 | C C | C T | T T | G G | G G | A G | G G |
| fluidigm.48- | -5.6823 | C T | C T | T T | A G | G G | A A | G G |
| fluidigm.48: | 13.0958 | C C | T T | T T | A G | G G | A A | G G |
| fluidigm. $48<$ | -4.1103 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm.48: | -1.1103 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 48 ¢ | -0.6384 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 48 ; | 7.4671 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 488 | -10.9042 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm.48s | -0.5680 | C C | T T | T T | A A | A G | A G | C G |
| fluidigm.49( | 9.0958 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.49] | -5.9042 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm.49- | -1.8443 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm.49: | -18.7196 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.49 | 5.3616 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.49: | -1.5680 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.49t | -6.7580 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.49; | 5.0958 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 49 ¢ | -1.9153 | C C | T T | T T | G G | A A | A A | G G |
| fluidigm.49s | -2.3841 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.50( | -2.6823 | C C | C C | T T | A A | G G | A G | G G |
| fluidigm.501 | -10.6823 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. $50-$ | -6.7580 | C T | T T | C T | A A | A G | A A | G G |
| fluidigm.50: | 5.2420 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm. $50<$ | 7.2420 | C C | C T | T T | A G | A G | A G | G G |
| fluidigm.50: | 4.6159 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 506 | -1.7580 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm.50; | 8.3177 | C C | C T | T T | A G | G G | A G | G G |
| fluidigm. 50 ¢ | -11.6823 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.50s | -14.1103 | C C | C C | T T | A A | G G | A A | C G |
| fluidigm.51( | -1.6384 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.511 | -0.9219 | C C | C T | T T | A G | G G | 00 | G G |
| fluidigm. 512 | 2.2804 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.51ः | -7.7580 | C C | C T | T T | A A | G G | A A | G G |


| fluidigm. $51<$ | -10.7196 | C C | T T | T T | A A | G G | A G | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm.51: | 9.2420 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm.51t | 6.8897 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.51\% | -3.6823 | C C | C T | T T | A A | G G | A G | G G |
| fluidigm. 51 \& | 3.2420 | C T | C C | T T | A G | A G | A A | G G |
| fluidigm.51s | 1.3616 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm. $52($ | -4.5680 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm.521 | 2.4320 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.52\% | -5.6823 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.52: | -9.6823 | C C | C T | T T | A G | A G | A G | C G |
| fluidigm.52 | 3.0958 | C C | C C | T T | A A | G G | A A | C G |
| fluidigm.52: | -0.5680 | C C | C C | T T | A G | A A | A A | C G |
| fluidigm.52t | 1.2420 | C C | T T | T T | G G | A A | A A | G G |
| fluidigm.52; | 7.1557 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 52$\}$ | 6.2420 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm.52s | 4.2420 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm.53( | 9.2420 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 531 | -10.1103 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm. 532 | 2.8897 | C C | C T | T T | A G | G G | A G | G G |
| fluidigm.53: | -4.7580 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.53< | 10.8897 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.53: | 7.3177 | C C | C T | T T | A G | A G | 00 | G G |
| fluidigm. $53 t$ | 4.0847 | C T | T T | C T | A G | G G | 00 | G G |
| fluidigm.53: | 12.0958 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm. 538 | 5.9847 | C C | C C | T T | A G | G G | A A | G G |
| fluidigm.53s | 8.2420 | C C | C C | T T | A G | 00 | A A | G G |
| fluidigm.54( | 4.0781 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm.541 | 5.8897 | C T | C T | T T | A G | A G | A A | G G |
| fluidigm.54^ | -5.6384 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm.54: | 1.6159 | C C | C T | C T | A A | G G | A G | G G |
| fluidigm.54 | -1.7580 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.54؛ | -0.9042 | C C | C T | T T | A G | A A | A A | G G |
| fluidigm.54t | 3.6159 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.54; | 6.4320 | C C | T T | T T | A A | G G | 00 | G G |
| fluidigm. 548 | -5.7580 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.54s | 4.2420 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm.55( | 0.2804 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 551 | 11.3177 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm. $55{ }^{\circ}$ | 5.3177 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.55: | 8.2420 | C C | C T | T T | A A | G G | A G | G G |
| fluidigm. 55 | -4.1103 | C C | T T | 00 | A A | G G | A A | G G |
| fluidigm.55: | 3.2804 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.55t | 6.4320 | C C | C T | T T | A A | G G | A A | G G |


| fluidigm. $55^{\circ}$ | -0.7196 | C C | T T | T T | A A | A G | A G | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm. 55 ¢ | 2.2420 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.55s | 0.0847 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm.56( | -4.7196 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.561 | -5.9153 | C C | C T | T T | A G | A G | A G | G G |
| fluidigm.562 | 7.2420 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.56: | -10.1103 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm. 56 | 5.9847 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.56: | -9.5680 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 566 | 2.2420 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.56: | 0.2804 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 568 | -2.7580 | C C | C C | T T | A G | A G | A A | G G |
| fluidigm.56؛ | 3.0958 | C T | C T | T T | A G | A G | A A | G G |
| fluidigm.57( | -14.6823 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 571 | -17.5680 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 572 | 1.0958 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm. 57 : | -11.7580 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm.57/ | -6.7580 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm.57: | -1.7196 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 57 t | 11.2420 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.57\% | 7.4320 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. $57 \%$ | -1.1103 | C C | C C | T T | A G | G G | A G | G G |
| fluidigm.57s | 1.3616 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 58 ( | 6.2420 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 581 | -16.5680 | CC | C C | T T | A G | G G | A A | G G |
| fluidigm.582 | 5.6159 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.58: | 3.0847 | C C | T T | T T | A A | A G | A G | C G |
| fluidigm.58< | -1.7196 | C C | T T | T T | A G | A A | A A | G G |
| fluidigm.58: | -0.6823 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm. 586 | 16.0958 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.58: | 6.0847 | C T | C C | T T | A A | A G | A A | G G |
| fluidigm. 588 | 1.2420 | C T | T T | T T | A A | A A | A A | G G |
| fluidigm.58s | 1.3616 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm.59( | 4.4671 | C T | T T | T T | G G | A A | A A | G G |
| fluidigm.591 | 3.8897 | C C | C C | T T | G G | A G | A A | G G |
| fluidigm.592 | 2.3616 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm.59: | 12.1557 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.59< | 3.8897 | C C | T T | T T | A G | A A | A A | G G |
| fluidigm.59: | 2.0847 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.59t | 4.2420 | C C | C T | C T | A G | A G | A A | G G |
| fluidigm.59; | -0.9042 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.59¢ | -6.7196 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm.59s | 4.2804 | C T | C T | T T | A A | A G | A A | C G |


| fluidigm. 600 | -1.6384 | C C | T T | T T | A A | G G | A A | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm.601 | -1.1103 | C C | C C | T T | A A | A G | A G | G G |
| fluidigm.60- | -3.5680 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.60: | -5.6384 | C C | C C | T T | A A | A A | A A | G G |
| fluidigm. $60<$ | 10.3177 | C C | T T | T T | A A | A G | A G | G G |
| fluidigm.60: | -1.6384 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 60 t | 3.3177 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.60: | -7.5680 | C C | C C | T T | A A | A A | A A | G G |
| fluidigm. 60 ¢ | -1.7580 | C C | T T | T T | G G | A G | A A | G G |
| fluidigm.60s | 3.3177 | C C | T T | T T | A G | G G | A G | G G |
| fluidigm.61( | 4.3177 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.611 | 3.1885 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.612 | -3.1103 | C C | C T | C T | A A | G G | A A | G G |
| fluidigm.61ः | -5.7580 | C T | C C | C T | A G | A G | A G | G G |
| fluidigm. $61<$ | -12.1103 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm.61: | -7.9042 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.61t | 11.8897 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.61; | -3.6823 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 618 | 9.8897 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.61s | -1.1103 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm.620 | 5.8897 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm.621 | 6.0847 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.62\% | 14.3616 | C C | T T | T T | A A | 00 | 00 | G G |
| fluidigm.62: | 3.0847 | C C | C C | T T | A A | A G | 00 | G G |
| fluidigm.62 | 4.2420 | C T | T T | T T | A G | A G | A A | G G |
| fluidigm.62: | -2.9153 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm. $62 t$ | 0.2420 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.62; | 10.9687 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 628 | -3.7196 | C C | C T | T T | A A | G G | A G | G G |
| fluidigm.62s | -1.5680 | C C | C T | T T | A G | A A | A A | G G |
| fluidigm. 631 | 3.3177 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 631 | -2.0313 | C C | C T | T T | A G | A G | A G | C G |
| fluidigm.632 | 9.2804 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.63: | -2.7580 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 63 | -5.1103 | C C | C C | C T | A G | G G | A A | G G |
| fluidigm.63: | -0.9042 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm. $63 t$ | 0.3616 | C T | T T | T T | A A | A G | A A | G G |
| fluidigm.63: | -2.5680 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm. 638 | -0.5680 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm.63s | 12.2420 | C C | C T | T T | A A | A G | A A | 00 |
| fluidigm.64( | 3.6159 | C T | C T | T T | A G | G G | A G | G G |
| fluidigm.641 | 11.2804 | C C | T T | T T | A A | A G | A G | G G |
| fluidigm.64^ | 1.1885 | C C | C T | T T | A G | G G | A A | G G |


| fluidigm.64: | -0.6823 | C C | T T | T T | A G | A G | A A | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm.64 | -6.1103 | C C | T T | T T | A G | A A | A A | G G |
| fluidigm.64: | -3.1103 | C C | C T | T T | A A | 00 | A A | G G |
| fluidigm.64t | -3.1103 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm.64: | -6.5680 | C C | C C | T T | A G | A G | A G | G G |
| fluidigm.64乏 | -2.7580 | C T | C T | T T | A G | G G | A A | G G |
| fluidigm.64! | 15.3177 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.65( | 1.2804 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm.651 | -0.1103 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.652 | 3.3616 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.65: | 23.0958 | C T | C T | T T | A A | A G | A A | G G |
| fluidigm.65 | -0.8115 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.65: | -7.8115 | C T | C C | T T | A A | A G | A A | G G |
| fluidigm.65t | 3.3616 | C T | T T | T T | A A | A G | A G | G G |
| fluidigm.65; | -11.1103 | C C | C C | T T | A G | A G | A A | G G |
| fluidigm. 65 ¢ | 8.3177 | C T | C T | T T | A G | A G | A A | G G |
| fluidigm.65s | -13.3841 | C C | T T | T T | A G | A G | A G | G G |
| fluidigm.660 | 6.1557 | C C | C C | T T | G G | A G | A A | G G |
| fluidigm.66] | -3.3841 | C C | T T | T T | A A | G G | G G | G G |
| fluidigm.662 | -10.1103 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.66: | 2.2420 | C C | T T | T T | G G | G G | A A | G G |
| fluidigm. 66 | 5.8897 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.66: | -12.6823 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm. $66 t$ | 10.9687 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.66: | 3.4320 | C C | T T | T T | A A | A G | A G | G G |
| fluidigm.66\& | 7.2804 | C C | T T | T T | A A | G G | A G | G G |
| fluidigm.66؛ | 4.3616 | C C | C T | T T | A A | A G | A A | C G |
| fluidigm.67( | -3.9042 | C C | C C | T T | A G | A G | A A | G G |
| fluidigm. 671 | 8.2420 | C C | C T | C T | A A | A A | A A | G G |
| fluidigm.672 | 5.9687 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.67: | 23.9687 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.67< | 1.9687 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm.67: | -0.3841 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm.67t | 1.3177 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm.67\% | -4.7196 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.67¢ | -2.5680 | C C | C C | T T | A A | A A | A A | G G |
| fluidigm.675 | 4.9687 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.68( | 0.3177 | C C | C T | T T | A A | G G | A G | G G |
| fluidigm. 681 | -8.7580 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm.682 | 17.8345 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm.68: | 1.2804 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.68 | 3.0958 | C T | C T | T T | A A | A G | A A | G G |
| fluidigm.68؛ | 5.8897 | C C | C T | T T | A A | G G | G G | G G |


| fluidigm. 68 t | 2.3616 | C C | T T | C T | G G | A G | A A | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm.68: | -4.6823 | C C | T T | T T | A A | G G | A G | G G |
| fluidigm. 688 | 2.3177 | C C | C T | T T | A G | A G | A G | C G |
| fluidigm.68s | -17.9042 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.69 | -14.1103 | C C | C T | T T | A A | A G | A A | C G |
| fluidigm.691 | 4.2804 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.692 | 3.2420 | C C | C T | C T | A A | G G | A A | G G |
| fluidigm.69: | 1.3616 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.69 | -15.1103 | C C | C C | T T | A A | G G | A G | G G |
| fluidigm.69: | -2.7196 | C C | C C | C T | A A | G G | A A | G G |
| fluidigm. 69 | -4.6823 | C C | T T | T T | G G | A G | A A | G G |
| fluidigm.69; | 2.6159 | C C | T T | T T | A G | G G | A A | G G |
| fluidigm. 69 ¢ | -6.7580 | C C | T T | T T | A A | A A | A A | G G |
| fluidigm.69s | 4.0958 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.700 | -1.0313 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.701 | -1.7196 | C T | C C | C T | A G | A G | A G | G G |
| fluidigm. $70-$ | -6.1103 | C C | T T | T T | A G | G G | A A | G G |
| fluidigm.70: | 2.8897 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm. $70<$ | 1.3616 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm.70: | -9.1103 | C T | C C | T T | A G | A G | A A | G G |
| fluidigm. 70 t | -10.7196 | C T | C C | T T | A G | G G | A G | G G |
| fluidigm.70: | -15.7580 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 70 ¢ | -7.9153 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm.70s | 4.2420 | C C | C T | T T | A A | A A | A G | G G |
| fluidigm.711 | 2.4320 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 711 | -3.6384 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.712 | -0.5680 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.71ः | 7.8897 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm. $71<$ | 2.9687 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.71؛ | 9.3177 | C C | C T | T T | G G | G G | A A | G G |
| fluidigm.71t | 1.2420 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm.71; | 1.4320 | T T | T T | T T | A G | A A | A A | G G |
| fluidigm.718 | 1.2420 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.71s | 1.8897 | C C | C C | T T | A A | A A | A A | G G |
| fluidigm. 721 | 3.0958 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.721 | -4.9042 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.72\% | 13.3177 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 72 : | 2.6159 | C C | C C | T T | A A | A A | A G | G G |
| fluidigm. 72 | 0.2420 | C C | C T | T T | A A | A G | A A | C G |
| fluidigm. 72 : | 12.8897 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm. $72 t$ | -1.7196 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 72 ; | 2.4320 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 72 \& | -5.6823 | C C | T T | C T | A G | G G | A A | G G |


| fluidigm.72 | -7.1103 | C C | C T | T T | A G | A A | A G | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm. 731 | 2.1885 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm. 731 | 2.8897 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.732 | 0.3177 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.73: | -0.5329 | C C | C C | C T | A A | A A | A A | 00 |
| fluidigm. $73<$ | 1.2804 | C C | C C | T T | A A | G G | A G | C G |
| fluidigm. 73 : | -7.7580 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm. $73 t$ | 1.2804 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.73: | -0.7196 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 738 | 12.3616 | C C | C T | T T | A A | A A | A G | G G |
| fluidigm.73s | 0.0958 | C C | T T | T T | A A | A A | A A | G G |
| fluidigm.74( | -12.1103 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.741 | 2.6159 | C C | C T | T T | A G | A G | A G | G G |
| fluidigm.74^2 | -6.5680 | C T | C T | T T | A G | A G | A G | G G |
| fluidigm.74: | 7.8897 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.74 | 5.2420 | C C | C T | T T | A G | A A | A A | G G |
| fluidigm. 74 ! | -1.7580 | C C | T T | T T | A G | G G | A A | G G |
| fluidigm. $74 \epsilon$ | -1.1103 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.74; | -2.1103 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 748 | -6.7196 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.74s | 4.0847 | C C | C T | C T | A A | A A | A G | G G |
| fluidigm.75( | 0.1557 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm.751 | -7.6384 | C C | C T | C T | A A | G G | A A | C G |
| fluidigm.75\% | 3.0847 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm.75: | 4.0958 | C C | C T | T T | A A | G G | A G | G G |
| fluidigm. 75 | -3.7580 | C T | T T | T T | G G | A A | A A | G G |
| fluidigm.75: | -6.6823 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm.75t | 1.4320 | C C | T T | T T | A G | A A | A G | G G |
| fluidigm. 75 ; | 1.4320 | C C | C C | T T | A A | A A | A A | G G |
| fluidigm. 75 ¢ | -8.1103 | C C | C C | T T | A A | A A | A A | G G |
| fluidigm.75s | -2.1103 | C C | T T | T T | A G | A A | A A | G G |
| fluidigm.760 | 5.9687 | C C | C T | T T | A A | A A | A G | G G |
| fluidigm. 761 | 6.8897 | C C | C C | T T | A G | A G | A G | G G |
| fluidigm.76: | -6.9153 | C C | C C | T T | A G | A A | A G | G G |
| fluidigm.76: | 0.8897 | C C | C T | T T | A G | A G | A G | G G |
| fluidigm. 76 | 4.1885 | C T | C C | T T | A A | A G | A A | G G |
| fluidigm.76: | -2.3841 | C T | T T | T T | A G | G G | A A | G G |
| fluidigm. $76 t$ | -4.6384 | C C | C C | T T | A G | A A | A A | G G |
| fluidigm. 76 ; | 5.2804 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 768 | 11.3177 | C C | C T | C T | A G | G G | A A | G G |
| fluidigm.76s | 4.2420 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.77( | 5.0958 | C C | C T | T T | A A | A A | A A | C G |
| fluidigm. 771 | -21.7580 | C C | T T | T T | A G | G G | A A | C G |


| fluidigm.772 | -13.1103 | C C | C T | T T | A A | A A | A A | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm.77: | -4.7196 | C C | C C | T T | A G | A A | A A | C G |
| fluidigm.77< | 0.8897 | C C | C C | T T | A A | A A | A A | G G |
| fluidigm.77! | -1.8443 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.77t | -12.9042 | C C | T T | C T | A A | A A | A A | G G |
| fluidigm.77\% | 4.3177 | C C | C T | T T | A A | A G | A A | C G |
| fluidigm.77¢ | 4.1885 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm.775 | 12.3177 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.78( | -1.7196 | C C | C T | T T | G G | A A | A G | G G |
| fluidigm. 781 | 13.1557 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.78: | -7.9153 | C C | C T | T T | G G | G G | A A | G G |
| fluidigm.78: | -3.9042 | C T | T T | C T | A A | A A | A A | G G |
| fluidigm.78< | -2.1103 | C C | T T | T T | A A | A A | A A | G G |
| fluidigm.78: | -6.0313 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm.78t | 12.1557 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.78: | -8.3841 | C C | T T | T T | G G | A G | A G | G G |
| fluidigm.78\& | -4.6823 | C T | C T | C T | A A | A G | A A | G G |
| fluidigm.78s | -3.5680 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.79( | 0.8897 | C C | C C | T T | A G | A G | A A | C G |
| fluidigm.79] | 0.4320 | C C | T T | T T | A G | G G | A A | C G |
| fluidigm.79: | -10.1103 | C C | C T | T T | A A | 00 | A A | C G |
| fluidigm.79: | -2.6384 | C C | T T | T T | A A | A A | A A | G G |
| fluidigm.79< | 9.2420 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.79؛ | -3.5680 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.79t | 13.2804 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.79; | 4.3616 | C C | T T | T T | A G | G G | A A | 00 |
| fluidigm. 798 | 4.4671 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.79s | -3.6384 | C C | T T | T T | A G | G G | A A | G G |
| fluidigm. 800 | 0.3177 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm.801 | 5.0958 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 80 - | -1.6384 | C T | C T | T T | A A | A G | A A | G G |
| fluidigm. 80 : | 11.8897 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm. $80<$ | -3.1103 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm. 80 ؛ | 19.0958 | C C | T T | T T | A G | G G | A G | G G |
| fluidigm. 80 t | 8.8897 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.80; | 5.2420 | C C | C C | T T | A A | G G | A G | G G |
| fluidigm. 80 ¢ | 9.0958 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 80 ¢ | 1.3616 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.81( | 3.1557 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.811 | 3.4671 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm.812 | -2.1655 | C C | C C | T T | A G | A A | A A | G G |
| fluidigm. 81 : | 11.2804 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm. $81<$ | -2.6823 | C T | C T | T T | A A | A G | A G | G G |


| fluidigm. 81 ¢ | 5.2420 | C C | T T | T T | A G | A A | A A | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm.81t | -5.7580 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. $81{ }^{\text {\% }}$ | -1.9042 | C C | C C | T T | A A | A G | A G | G G |
| fluidigm. 818 | 13.0847 | C C | C C | T T | A G | A G | A G | G G |
| fluidigm.81s | 14.3177 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm. $82($ | -10.9042 | C C | C C | T T | A A | A A | A A | G G |
| fluidigm.821 | 11.3177 | C C | C C | T T | A A | A G | A A | C G |
| fluidigm. $82{ }^{2}$ | 1.9687 | C C | C T | T T | A G | A G | A G | G G |
| fluidigm.82: | -0.1103 | C C | C T | C T | A A | G G | A A | G G |
| fluidigm.82 | 1.2420 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 82 : | -0.6384 | C T | C T | T T | A G | G G | A A | G G |
| fluidigm. 82 t | -1.3841 | C C | C C | T T | A A | A A | A A | G G |
| fluidigm. 82 ; | -1.7580 | C T | C T | T T | A G | G G | A A | G G |
| fluidigm. 82 \& | -7.1103 | C C | C C | T T | A A | A G | A A | C G |
| fluidigm.82s | 1.1885 | C C | T T | T T | A A | A A | A A | G G |
| fluidigm.83( | 7.2804 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 831 | 1.2420 | C C | T T | T T | A G | G G | A G | G G |
| fluidigm.832 | 3.4320 | C C | T T | T T | A G | A A | A G | G G |
| fluidigm.83: | 6.3177 | C C | C C | T T | A A | A A | A A | G G |
| fluidigm. 83 | -0.7580 | C C | T T | T T | A A | A A | A G | G G |
| fluidigm.83: | 0.0958 | C C | C T | T T | A G | A A | A A | G G |
| fluidigm.83t | -13.7580 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.83; | -2.6384 | C C | C T | T T | A A | G G | A G | G G |
| fluidigm.838 | 9.2804 | C C | T T | T T | A A | G G | A G | C G |
| fluidigm.83s | -2.5680 | C C | T T | T T | A A | G G | A A | C G |
| fluidigm. $84($ | -0.6823 | C C | T T | T T | A G | G G | A A | C G |
| fluidigm. 841 | 3.4671 | C C | T T | T T | A A | G G | A A | C G |
| fluidigm. $84{ }^{\text {e }}$ | 0.0847 | C C | C T | T T | G G | G G | 00 | G G |
| fluidigm. 84 : | -3.7580 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 84 | 2.0958 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm. 84 ! | -26.6823 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. $84 \%$ | -0.9153 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm. 84 ; | 8.4320 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 848 | 10.3177 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.84¢ | -12.6823 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.85( | -2.7196 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.851 | -4.7196 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. $85{ }^{\circ}$ | 8.8897 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.85: | 6.1885 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 85 | -2.7580 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.85: | -8.7196 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.85t | 7.6159 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm. $85{ }^{\circ}$ | 1.8897 | C C | C C | T T | A G | G G | A A | G G |


| fluidigm. 858 | 11.0958 | C C | C T | T T | A A | A A | A A | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm.85s | -0.3841 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.860 | -4.1103 | C C | C C | T T | A G | A A | A A | C G |
| fluidigm.861 | -2.5680 | C C | T T | T T | A G | G G | A A | G G |
| fluidigm.86- | -6.1103 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.86: | 0.8897 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 86 | 4.0958 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm.86: | 0.3177 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm.86t | -7.3841 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm.86; | -0.5680 | C C | C C | T T | A G | G G | A A | G G |
| fluidigm. 868 | -3.6384 | C C | C T | T T | A A | A G | A A | C G |
| fluidigm.86s | -0.7580 | C C | C T | C T | A G | G G | A G | G G |
| fluidigm.87( | 3.2420 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm. 871 | -9.5680 | C C | T T | T T | A G | G G | A A | C G |
| fluidigm.872 | 10.3177 | C C | T T | T T | A G | G G | A G | G G |
| fluidigm.87: | 0.4320 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. $87<$ | 10.2420 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm. 87 \% | 3.2420 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 87 t | -0.0313 | C C | C T | T T | A A | A A | 00 | G G |
| fluidigm.87\% | 5.9847 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 878 | 6.3177 | C C | C C | C T | A A | A A | A A | G G |
| fluidigm.87s | 0.3177 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.88( | 11.2804 | C T | C T | T T | A A | G G | A A | G G |
| fluidigm. 881 | 0.2420 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm. $88{ }^{\circ}$ | 1.3616 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.88: | -3.3841 | C C | C T | T T | A A | G G | A G | G G |
| fluidigm.88 | 10.0847 | C T | T T | T T | A G | A A | A A | G G |
| fluidigm.88: | -1.6823 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.88t | -9.5680 | C T | C T | T T | A A | G G | A A | G G |
| fluidigm.88: | 11.6159 | C C | C T | T T | A A | G G | A G | G G |
| fluidigm. 888 | -8.6823 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.88s | 13.0781 | C C | C T | T T | A A | A G | A G | C G |
| fluidigm.89( | -14.1103 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.89] | -4.1103 | C C | C T | T T | A G | A G | A G | G G |
| fluidigm.89- | 6.9847 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.89: | 1.8897 | C C | C T | C T | A A | G G | 00 | G G |
| fluidigm. 89 | 2.2420 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm.89: | 8.3177 | C C | C T | T T | A G | G G | A G | G G |
| fluidigm. 89 ¢ | -0.9042 | C C | T T | C T | A A | A G | A A | G G |
| fluidigm.89; | 6.2804 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm. 89 ¢ | 8.3616 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.89s | -1.8115 | C T | C T | T T | A A | A G | A A | G G |
| fluidigm.90( | -25.9042 | C C | T T | C T | A G | G G | A A | G G |


| fluidigm. 901 | -4.9153 | C C | C T | T T | A A | G G | A A | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm. $90-$ | 4.1557 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.90: | -3.6823 | C C | C T | T T | A A | G G | A G | G G |
| fluidigm. $90<$ | -5.6823 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm.90: | -3.9042 | T T | C T | T T | A A | A G | A A | G G |
| fluidigm. 900 | 11.8897 | C C | T T | T T | A G | A G | A A | C G |
| fluidigm.90: | 8.3177 | C C | C T | T T | A A | A A | A G | G G |
| fluidigm. 90 ¢ | 1.0847 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 90 S | 8.3177 | C T | T T | T T | A G | A G | A G | G G |
| fluidigm.91( | 7.3616 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm. 911 | 2.2420 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm. 912 | -7.5680 | C T | T T | T T | A G | A A | A A | G G |
| fluidigm.91: | -2.6823 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm. $91<$ | -5.5680 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm. 91 : | -6.5680 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 91 ( | -1.9153 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.91; | 7.3177 | C C | C C | T T | A G | A G | A A | G G |
| fluidigm. 918 | 1.2420 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.91s | 13.2420 | C C | C C | T T | A G | G G | A A | G G |
| fluidigm.920 | 0.0958 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.92] | 13.2420 | C C | T T | C T | A A | A A | A A | G G |
| fluidigm.92\% | -7.7580 | C C | T T | T T | A A | A A | A G | G G |
| fluidigm.92: | -7.7580 | C C | T T | T T | A G | A G | A G | G G |
| fluidigm.92 | -5.7196 | C C | C T | T T | G G | G G | A A | G G |
| fluidigm.92: | -7.9153 | C C | T T | T T | G G | G G | A A | G G |
| fluidigm. 92 t | 0.3177 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.92; | 3.8897 | C C | T T | T T | A A | A G | A G | G G |
| fluidigm. 928 | -12.6823 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm.92s | 1.2420 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm. 931 | -6.9042 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 931 | -4.6384 | T T | C C | T T | A A | G G | A A | G G |
| fluidigm.932- | 7.2420 | C C | T T | T T | A G | A G | A G | G G |
| fluidigm.93: | 0.4320 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 93 | 3.4671 | C C | C T | C T | A A | G G | A A | G G |
| fluidigm.93: | 4.2804 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.93t | 2.4320 | C T | C T | T T | A A | G G | A A | G G |
| fluidigm.93: | 1.0847 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. 938 | -1.1103 | C C | T T | C T | G G | A G | A A | G G |
| fluidigm.93s | 9.2420 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.94( | 2.8897 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm.941 | 10.2420 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm.94^ | 12.2420 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.94: | 4.2420 | C C | C T | T T | A G | G G | A A | G G |


| fluidigm.94 | -1.9042 | C C | T T | T T | A A | A G | A A | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm. 94 ! | 3.8897 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm. 944 | 10.9687 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.94; | 0.8897 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm. 94 ¢ | 6.2420 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.94! | -0.1103 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm.95( | -14.1103 | C C | T T | T T | G G | A G | A A | G G |
| fluidigm. 951 | 6.0781 | C C | T T | T T | A A | G G | G G | G G |
| fluidigm.95\% | 13.0958 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.95: | 5.3177 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 95 | 17.3177 | C C | C C | T T | A G | A G | A A | G G |
| fluidigm.95: | 13.8897 | C C | 00 | T T | A A | A G | A A | G G |
| fluidigm. 95 ( | 1.4320 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.95; | -2.8443 | C C | C T | T T | A A | A G | A G | G G |
| fluidigm. 958 | -8.7580 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.95s | -1.7580 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.960 | -2.6823 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.961 | -3.6384 | T T | C C | T T | A A | A A | A A | G G |
| fluidigm.96- | -4.7580 | C C | C C | T T | 00 | A G | A A | G G |
| fluidigm.96: | -0.7580 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 96 | -0.7580 | C T | 00 | C T | G G | A G | A G | G G |
| fluidigm.96: | -7.7196 | C T | C T | T T | 00 | A G | A A | G G |
| fluidigm.96t | -1.3841 | C C | C T | T T | A G | A A | A G | G G |
| fluidigm.96: | 10.2420 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm. 96 ¢ | 12.8897 | C C | T T | T T | A A | A G | G G | G G |
| fluidigm.96s | -0.6384 | C C | C C | T T | A G | A G | A A | G G |
| fluidigm.97( | 3.0958 | C C | T T | T T | A G | G G | A A | G G |
| fluidigm. 971 | 4.0847 | C C | C T | T T | 00 | G G | A A | G G |
| fluidigm. 972 | -1.5680 | C C | 00 | T T | A A | A G | A G | G G |
| fluidigm.97: | 3.2804 | C C | C T | T T | A G | A G | A G | G G |
| fluidigm.97< | 1.0958 | C T | C T | T T | A A | G G | A G | G G |
| fluidigm.97: | -3.6823 | C C | T T | T T | A G | A A | A A | G G |
| fluidigm. 97 t | 8.8897 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm.97: | -6.7580 | C T | T T | T T | 00 | G G | A G | G G |
| fluidigm. 978 | 10.0781 | C C | C T | T T | A A | G G | A G | G G |
| fluidigm.97s | -1.6823 | C C | T T | C T | G G | A G | A A | G G |
| fluidigm. 981 | -4.5680 | C C | T T | T T | A G | A G | A A | C G |
| fluidigm. 981 | -4.6384 | C C | T T | T T | A G | G G | A A | C G |
| fluidigm.98: | -5.7196 | C C | C T | T T | G G | G G | A G | G G |
| fluidigm.98: | 0.8897 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm. 98 < | 1.8897 | C C | 00 | T T | A A | G G | A A | G G |
| fluidigm.98: | 0.8897 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm.98t | -13.7580 | C C | C C | T T | A A | G G | A A | G G |


| fluidigm.98: | 12.3177 | C C | C T | T T | A G | A A | A A | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm. 988 | -8.3841 | C T | 00 | T T | A A | A G | A A | C G |
| fluidigm.98s | -6.5680 | C C | C C | T T | A A | A A | 00 | G G |
| fluidigm. 990 | -1.6384 | C C | T T | C T | A A | G G | 00 | G G |
| fluidigm.99] | 11.0958 | C C | C T | T T | 00 | A G | A A | G G |
| fluidigm.99* | 2.8897 | C C | 00 | T T | A A | G G | A A | G G |
| fluidigm.99: | 3.9847 | C C | T T | C T | A G | A G | A A | G G |
| fluidigm. 99 | -12.6823 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm.99: | -1.5680 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm. 99 t | -5.7580 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm.99; | -2.6823 | C C | 00 | T T | A G | G G | A G | G G |
| fluidigm. 99 ع | -12.9042 | C C | C T | T T | A A | A G | A A | 00 |
| fluidigm.99s | -6.9042 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm.100 | -2.3841 | C C | C C | T T | A A | A A | A A | G G |
| fluidigm.100 | 14.3616 | C C | C C | C T | A G | A G | A A | G G |
| fluidigm.100 | 3.1557 | C C | C C | T T | A G | A G | A A | G G |
| fluidigm.100 | 4.2420 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.100 | 6.0958 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm.100 | 0.2804 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.100 | -5.1103 | C C | 00 | T T | A A | A G | A A | G G |
| fluidigm.100 | 6.0958 | C C | T T | T T | A G | A G | A G | G G |
| fluidigm.100 | -1.7580 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm.100 | 0.8897 | C C | C T | T T | A A | G G | A G | G G |
| fluidigm.10] | 0.1557 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 101 | 4.0847 | C C | T T | T T | G G | G G | A G | G G |
| fluidigm. 101 | 10.2420 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm. 101 | 4.0847 | C C | 00 | T T | A G | A G | A G | G G |
| fluidigm. 101 | 0.8897 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm. 101 | -0.1103 | C C | C T | T T | A A | G G | A G | C G |
| fluidigm. 101 | -15.9042 | C C | C T | T T | A G | G G | A G | G G |
| fluidigm. 101 | 14.4320 | C C | C T | T T | G G | A G | A A | G G |
| fluidigm.101 | -5.5680 | C C | C C | T T | A A | A G | A G | G G |
| fluidigm.101 | -6.7196 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm. $10-$ | -3.7196 | C C | T T | T T | A A | A A | A A | G G |
| fluidigm. $10-$ | 12.0847 | C C | C T | T T | A A | G G | 00 | G G |
| fluidigm. 102 | 14.2804 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm. $10^{-}$ | 3.8897 | C C | C T | T T | A A | A A | A A | G G |
| fluidigm. 102 | -4.7196 | C C | C T | T T | A G | G G | A G | G G |
| fluidigm. 102 | 7.3177 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm. 102 | -13.7196 | C C | T T | T T | A G | A A | A G | G G |
| fluidigm. 102 | 0.8897 | C C | T T | T T | A A | A A | A A | G G |
| fluidigm. 102 | 10.9687 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm. $10 \sim$ | 2.0958 | C C | C T | T T | A G | A G | A A | G G |


| fluidigm.10: | 1.2804 | C C | C C | T T | A G | G G | A G | G G |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| fluidigm. 10 : | -14.6823 | C C | C T | C T | A G | G G | A A | G G |
| fluidigm. 10 : | 2.2804 | C C | C C | T T | A G | G G | A A | G G |
| fluidigm. 10 : | -10.7196 | C C | C T | T T | A G | A A | A A | G G |
| fluidigm. 10 : | -10.7580 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm. 10 : | 6.3616 | C C | C T | T T | A G | G G | A A | G G |
| fluidigm.10: | -0.6384 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm.10: | 3.2420 | C C | C T | T T | A G | A G | A G | G G |
| fluidigm.10: | -15.9042 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm.10: | 2.1885 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. $10<$ | 1.3616 | C C | T T | T T | A A | A A | A A | G G |
| fluidigm. $10<$ | -2.1103 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. $10<$ | 5.4320 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 10 | 12.4671 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 10 | -3.7196 | C C | C T | T T | A A | G G | A A | C G |
| fluidigm. 10 | 2.0958 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 10 | -2.0313 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm. 10 | 19.3177 | C C | C T | T T | A A | G G | A A | G G |
| fluidigm. $10<$ | -7.7196 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. $10<$ | -0.9153 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.10: | -10.7196 | C C | C T | C T | A G | A A | A G | G G |
| fluidigm.10: | 6.9687 | C C | T T | T T | A G | A G | A G | G G |
| fluidigm.10: | -10.6823 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm.10: | -6.6384 | C C | C C | T T | A A | G G | A A | G G |
| fluidigm.10: | 9.2420 | C C | C T | T T | A A | G G | A G | G G |
| fluidigm.10: | 4.3177 | C C | C T | T T | A G | A G | A A | C G |
| fluidigm.10: | 0.2804 | C C | C T | T T | A A | G G | A G | G G |
| fluidigm.10: | -6.6384 | C C | T T | T T | A A | G G | A A | G G |
| fluidigm.10: | 21.0958 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.10: | -9.1103 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm. 106 | -0.9153 | C C | T T | T T | A A | G G | A G | G G |
| fluidigm. 106 | -6.5680 | C C | T T | T T | A G | A G | A A | G G |
| fluidigm. 10 t | -1.6384 | C C | C T | T T | A G | A G | A A | G G |
| fluidigm. 106 | 8.8345 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm. 106 | 1.3177 | C T | C T | T T | A G | G G | A A | G G |
| fluidigm. 106 | -1.9153 | C C | C C | T T | A A | A G | A A | G G |
| fluidigm. 106 | 0.3177 | C C | C T | T T | A A | G G | A G | G G |
| fluidigm. 106 | -4.5680 | C C | C T | T T | A A | A G | A A | C G |
| fluidigm. 106 | -5.6823 | C T | T T | C T | A A | G G | A A | G G |
| fluidigm. 106 | -1.7580 | C C | T T | T T | A A | A G | A A | G G |
| fluidigm.10; | -8.7580 | C T | C T | C T | A A | A A | A A | G G |
| fluidigm.10: | 5.2420 | C C | C T | T T | A A | A G | A A | G G |
| fluidigm.10; | -2.1103 | C C | T T | T T | A A | G G | A A | G G |

Table S2. SNPs analyzed in replication samples and for polygenic modification score.
From Fluidigm genotype data, 61 independent SNPs were chosen to be analyzed for polygenic modification score. S Use of the Fluidigm platform for replication analysis required us to choose 96 SNPs as a single genotyping panel, an MAF, minor allele frequency; HWE, Hardy-Weinberg equilibrium

| SNP | Chromosome | BP (hg 19) | Minor allele | Major allele | Discovery set (GWA) |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  | MAF | ffect size / minor alle | P -value |
| rs113605276 | 1 | 8,623,490 | T | C | 0.046 | -0.83 | $3.90 \mathrm{E}-02$ |
| rs1146382 | 1 | 85,918,101 | C | T | 0.417 | 0.65 | $8.11 \mathrm{E}-05$ |
| rs115068682 | 1 | 108,450,969 | C | T | 0.035 | -2.02 | $4.49 \mathrm{E}-06$ |
| rs45576236 | 1 | 112,319,388 | G | A | 0.194 | 0.71 | $1.03 \mathrm{E}-03$ |
| rs3820400 | 1 | 168,074,746 | A | G | 0.388 | 0.78 | $1.19 \mathrm{E}-05$ |
| rs10159075 | 1 | 204,160,370 | G | A | 0.091 | -0.89 | $1.88 \mathrm{E}-03$ |
| rs75376497 | 1 | 248,086,661 | C | G | 0.035 | -2.05 | $3.44 \mathrm{E}-06$ |
| rs14474193: | 2 | 11,230,267 | A | C | 0.017 | -2.86 | 4.44E-06 |
| rs4854546 | 2 | 69,317,925 | G | A | 0.109 | -0.93 | 5.22E-04 |
| rs72810940 | 2 | 75,555,265 | A | G | 0.029 | 2.43 | $5.88 \mathrm{E}-07$ |
| rs6751149 | 2 | 127,924,981 | C | T | 0.476 | 0.65 | $2.20 \mathrm{E}-05$ |
| rs778194 | 2 | 137,599,040 | C | A | 0.469 | 0.59 | $4.97 \mathrm{E}-04$ |
| rs13017290 | 2 | 202,909,097 | C | T | 0.477 | 0.69 | $3.93 \mathrm{E}-05$ |
| rs17036872 | 3 | 12,559,188 | A | G | 0.167 | -0.90 | $2.54 \mathrm{E}-05$ |
| rs17197692 | 3 | 36,775,946 | C | A | 0.059 | -1.38 | $6.33 \mathrm{E}-05$ |
| rs1799977 | 3 | 37,053,568 | G | A | 0.319 | 0.90 | 7.16E-07 |
| rs34625289 | 3 | 64,696,009 | A | G | 0.111 | -0.97 | $1.92 \mathrm{E}-04$ |
| rs1491738 | 3 | 68,276,485 | T | C | 0.286 | 0.69 | $7.87 \mathrm{E}-05$ |
| rs2289596 | 3 | 111,701,173 | C | T | 0.207 | 0.57 | $1.13 \mathrm{E}-02$ |
| rs7652523 | 3 | 171,674,996 | C | G | 0.389 | 0.60 | $7.29 \mathrm{E}-04$ |
| rs7627373 | 3 | 190,763,662 | A | G | 0.168 | -0.89 | $1.03 \mathrm{E}-04$ |
| rs890490 | 3 | 196,750,207 | A | G | 0.197 | 0.81 | $4.22 \mathrm{E}-05$ |
| rs77304846 | 4 | 70,495,353 | C | T | 0.182 | -0.74 | 6.14E-04 |
| rs143869898 | 4 | 105,077,431 | A | G | 0.015 | -3.05 | $1.72 \mathrm{E}-05$ |
| rs10005354 | 4 | 167,869,220 | G | T | 0.098 | 1.07 | $7.70 \mathrm{E}-05$ |
| rs72713682 | 4 | 178,684,282 | C | T | 0.018 | -2.61 | $1.53 \mathrm{E}-05$ |
| rs12655177 | 5 | 2,156,456 | T | C | 0.108 | 1.10 | $1.48 \mathrm{E}-05$ |
| rs7704337 | 5 | 113,670,134 | G | A | 0.266 | 0.80 | $2.58 \mathrm{E}-05$ |
| rs79274321 | 5 | 121,660,713 | A | G | 0.058 | -1.42 | $3.70 \mathrm{E}-05$ |
| rs67972044 | 5 | 155,987,761 | C | G | 0.052 | -1.67 | $4.91 \mathrm{E}-06$ |
| rs13157017 | 5 | 156,610,285 | C | T | 0.028 | -2.12 | $2.31 \mathrm{E}-05$ |
| rs11577580\& | 5 | 159,350,164 | T | C | 0.023 | -2.45 | $5.59 \mathrm{E}-06$ |
| rs9466071 | 6 | 21,392,004 | A | G | 0.364 | 0.65 | $1.49 \mathrm{E}-04$ |
| rs6934819 | 6 | 132,095,805 | A | C | 0.069 | -1.49 | $2.81 \mathrm{E}-06$ |
| rs1247336 | 6 | 161,377,557 | C | T | 0.245 | -0.86 | $2.14 \mathrm{E}-05$ |
| rs917810 | 7 | 21,061,360 | G | C | 0.383 | 0.74 | $3.17 \mathrm{E}-05$ |
| rs701280 | 7 | 83,533,062 | T | C | 0.446 | -0.44 | 6.58E-03 |
| rs79959239 | 7 | 131,887,315 | T | C | 0.011 | 3.18 | $2.98 \mathrm{E}-05$ |


| rs116940312 | 8 | 9,230,961 | G | C | 0.035 | 1.92 | 7.14E-05 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| rs9325798 | 8 | 16,644,586 | C | T | 0.021 | 2.41 | $1.54 \mathrm{E}-05$ |
| rs16896685 | 8 | 99,155,532 | A | G | 0.125 | -1.04 | $2.99 \mathrm{E}-05$ |
| rs34852161 | 8 | 103,284,508 | A | C | 0.083 | -1.48 | $3.43 \mathrm{E}-07$ |
| rs7837873 | 8 | 125,225,255 | A | G | 0.397 | 0.74 | $3.54 \mathrm{E}-05$ |
| rs 14841492, | 9 | 92,077,451 | A | G | 0.028 | -1.74 | $2.72 \mathrm{E}-04$ |
| rs12412337 | 10 | 113,652,642 | A | G | 0.049 | 1.53 | $8.60 \mathrm{E}-05$ |
| rs14894275 | 11 | 43,738,055 | C | T | 0.014 | -3.12 | $6.33 \mathrm{E}-06$ |
| rs15042945 | 11 | 58,854,570 | G | A | 0.023 | 2.21 | $5.77 \mathrm{E}-05$ |
| rs481871 | 11 | 79,354,702 | A | G | 0.095 | -1.21 | $8.21 \mathrm{E}-06$ |
| rs10892160 | 11 | 117,552,640 | G | A | 0.194 | -0.80 | 9.95E-05 |
| rs11062045 | 12 | 2,098,435 | T | A | 0.144 | 1.01 | $1.42 \mathrm{E}-05$ |
| rs15039340, | 15 | 31,202,961 | A | G | 0.016 | -5.55 | $0.00 \mathrm{E}-16$ |
| rs35811129 | 15 | 31,241,346 | A | G | 0.272 | 1.38 | $1.16 \mathrm{E}-13$ |
| rs61064919 | 16 | 13,343,332 | T | G | 0.190 | -0.88 | 2.05E-05 |
| rs16975803 | 16 | 23,051,026 | T | C | 0.363 | 0.68 | 6.24E-05 |
| rs1486437 | 16 | 51,899,860 | G | A | 0.116 | -1.19 | $2.03 \mathrm{E}-06$ |
| rs74611520 | 16 | 56,981,126 | T | G | 0.112 | 1.08 | $4.51 \mathrm{E}-05$ |
| rs72863909 | 18 | 1,700,716 | G | C | 0.102 | -1.07 | $1.13 \mathrm{E}-04$ |
| rs80324765 | 18 | 43,344,674 | A | G | 0.077 | -0.99 | $2.61 \mathrm{E}-03$ |
| rs6136301 | 20 | 18,108,215 | T | A | 0.055 | -1.50 | $2.07 \mathrm{E}-05$ |
| rs62215296 | 20 | 24,564,646 | A | G | 0.278 | 0.59 | $2.31 \mathrm{E}-03$ |
| rs738972 | 22 | 33,986,668 | C | T | 0.205 | -0.76 | $1.29 \mathrm{E}-04$ |

ingle SNP association analysis results in the Fluidigm data are shown.
$d$ therefore we selected SNPs based on relatively relaxed criteria that considered nominal association significance in e

| Replication set (Fluidigm) |  |  |  |  | Meta-analysis |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Call rate (\%) | HWE $p$-value | MAF | ffect size / minor alle | P -value | P -value | Nearest gene(s) |
| 100.0 | $1.2 \mathrm{E}-01$ | 0.046 | 0.09 | $8.27 \mathrm{E}-01$ | $1.65 \mathrm{E}-012$ | RERE |
| 97.2 | $6.9 \mathrm{E}-01$ | 0.413 | -0.11 | $5.51 \mathrm{E}-01$ | $1.08 \mathrm{E}-02 \mathrm{D}$ | DDAH1 |
| 99.7 | $3.9 \mathrm{E}-01$ | 0.043 | 0.02 | $9.69 \mathrm{E}-01$ | $7.14 \mathrm{E}-04$ | VAV3 |
| 98.3 | $2.3 \mathrm{E}-01$ | 0.178 | -0.25 | $2.93 \mathrm{E}-01$ | $8.06 \mathrm{E}-02 \mathrm{~K}$ | KCND3 |
| 99.4 | $2.9 \mathrm{E}-01$ | 0.387 | 0.00 | $9.84 \mathrm{E}-01$ | $1.07 \mathrm{E}-03$ | GPR161 |
| 93.0 | $2.3 \mathrm{E}-01$ | 0.090 | 0.03 | $9.32 \mathrm{E}-01$ | $2.20 \mathrm{E}-02$ | KISS1 |
| 99.2 | $5.8 \mathrm{E}-01$ | 0.033 | -0.39 | $4.47 \mathrm{E}-01$ | $7.40 \mathrm{E}-05$ | OR2T8 |
| 99.9 | $3.1 \mathrm{E}-01$ | 0.011 | -0.02 | $9.79 \mathrm{E}-01$ | $6.08 \mathrm{E}-04 \mathrm{H}$ | FLJ33534 |
| 95.7 | $4.3 \mathrm{E}-01$ | 0.114 | 0.68 | $2.11 \mathrm{E}-02$ | $2.81 \mathrm{E}-01$ | ANTXR1 |
| 99.9 | $6.4 \mathrm{E}-01$ | 0.020 | -0.33 | $6.17 \mathrm{E}-01$ | $7.32 \mathrm{E}-04$ | TACRI |
| 99.4 | $6.2 \mathrm{E}-01$ | 0.476 | 0.44 | $1.62 \mathrm{E}-02$ | $1.90 \mathrm{E}-06$ | CYP27C1 |
| 97.6 | $2.6 \mathrm{E}-01$ | 0.479 | -0.04 | $8.41 \mathrm{E}-01$ | $1.36 \mathrm{E}-02$ | THSD7B |
| 99.8 | $3.3 \mathrm{E}-01$ | 0.469 | -0.11 | $5.49 \mathrm{E}-01$ | $7.93 \mathrm{E}-03 \mathrm{~F}$ | FZD7 |
| 99.5 | $7.0 \mathrm{E}-02$ | 0.153 | 0.02 | $9.23 \mathrm{E}-01$ | $2.16 \mathrm{E}-03$ | TSEN2 |
| 99.5 | $3.7 \mathrm{E}-01$ | 0.063 | 0.16 | $6.66 \mathrm{E}-01$ | $7.22 \mathrm{E}-03 \mathrm{D}$ | DCLK3 |
| 99.7 | $6.8 \mathrm{E}-01$ | 0.305 | 0.59 | $2.58 \mathrm{E}-03$ | $1.19 \mathrm{E}-081$ | MLH1 |
| 99.5 | $3.9 \mathrm{E}-01$ | 0.115 | 0.17 | $5.61 \mathrm{E}-01$ | $1.71 \mathrm{E}-02$ | ADAMTS9-AS2 |
| 98.0 | $6.1 \mathrm{E}-01$ | 0.296 | 0.01 | $9.56 \mathrm{E}-01$ | $2.86 \mathrm{E}-03$ | FAM19A1 |
| 97.9 | $3.6 \mathrm{E}-02$ | 0.198 | 0.33 | $1.39 \mathrm{E}-01$ | $4.03 \mathrm{E}-03$ | ABHD10 |
| 95.7 | $9.8 \mathrm{E}-02$ | 0.381 | -0.10 | $5.99 \mathrm{E}-01$ | $2.88 \mathrm{E}-02$ | TMEM212-AS1 |
| 98.3 | $9.5 \mathrm{E}-01$ | 0.179 | 0.00 | $9.96 \mathrm{E}-01$ | $3.82 \mathrm{E}-03$ | OSTN |
| 99.3 | $6.2 \mathrm{E}-01$ | 0.196 | 0.03 | $8.99 \mathrm{E}-01$ | $1.74 \mathrm{E}-03$ | MELTF |
| 98.3 | $6.2 \mathrm{E}-01$ | 0.171 | -0.05 | $8.50 \mathrm{E}-01$ | $7.35 \mathrm{E}-03$ | UGT2A1 / UGT2A2 |
| 99.6 | $1.2 \mathrm{E}-01$ | 0.006 | 1.13 | $3.19 \mathrm{E}-01$ | $1.14 \mathrm{E}-02$ | CXXC4 |
| 97.7 | $1.4 \mathrm{E}-02$ | 0.086 | 0.06 | $8.60 \mathrm{E}-01$ | $2.15 \mathrm{E}-03$ | SPOCK3 |
| 99.5 | $2.3 \mathrm{E}-02$ | 0.018 | 0.03 | $9.61 \mathrm{E}-01$ | $1.46 \mathrm{E}-03 \mathrm{~L}$ | LINC01098 |
| 99.6 | $2.7 \mathrm{E}-01$ | 0.105 | 0.07 | $8.06 \mathrm{E}-01$ | $7.13 \mathrm{E}-04 \mathrm{~L}$ | LOC100506858 |
| 100.0 | $2.5 \mathrm{E}-01$ | 0.267 | -0.12 | $5.52 \mathrm{E}-01$ | $6.37 \mathrm{E}-03 \mathrm{~K}$ | KCNN2 |
| 94.7 | $3.9 \mathrm{E}-01$ | 0.067 | 0.52 | $1.64 \mathrm{E}-01$ | $2.90 \mathrm{E}-02$ | SNCAIP |
| 99.4 | $2.6 \mathrm{E}-01$ | 0.049 | -0.03 | $9.52 \mathrm{E}-01$ | $5.85 \mathrm{E}-04$ | SGCD |
| 99.4 | $1.6 \mathrm{E}-01$ | 0.025 | 0.07 | $8.99 \mathrm{E}-01$ | $2.19 \mathrm{E}-03$ | ITK |
| 99.2 | $3.7 \mathrm{E}-01$ | 0.020 | 0.88 | $1.77 \mathrm{E}-01$ | $1.32 \mathrm{E}-02$ | ADRA1B |
| 98.4 | $5.8 \mathrm{E}-02$ | 0.361 | -0.17 | $3.53 \mathrm{E}-01$ | $2.72 \mathrm{E}-02 \mathrm{~L}$ | LINC00581 |
| 98.5 | $2.3 \mathrm{E}-01$ | 0.062 | -0.03 | $9.37 \mathrm{E}-01$ | $3.94 \mathrm{E}-04 \mathrm{~L}$ | ENPP3 |
| 97.3 | $4.7 \mathrm{E}-01$ | 0.244 | -0.18 | $3.94 \mathrm{E}-01$ | $1.82 \mathrm{E}-04$ | MAP3K4 |
| 98.9 | $1.7 \mathrm{E}-01$ | 0.382 | 0.20 | $2.85 \mathrm{E}-01$ | $1.37 \mathrm{E}-04 \mathrm{~L}$ | LINC01162 |
| 94.9 | $8.9 \mathrm{E}-01$ | 0.452 | 0.11 | $5.60 \mathrm{E}-01$ | $9.74 \mathrm{E}-02$ | SEMA3A |
| 98.3 | $1.0 \mathrm{E}+00$ | 0.010 | 0.32 | 7.28E-01 | $8.22 \mathrm{E}-04$ P | PLXNA4 |


| 99.9 | $2.9 \mathrm{E}-01$ |
| ---: | ---: |
| 93.1 | $2.9 \mathrm{E}-01$ |
| 98.7 | $6.3 \mathrm{E}-01$ |
| 100.0 | $3.6 \mathrm{E}-01$ |
| 97.5 | $2.8 \mathrm{E}-02$ |
| 94.3 | $1.3 \mathrm{E}-01$ |
| 99.6 | $8.5 \mathrm{E}-01$ |
| 99.9 | $1.0 \mathrm{E}+00$ |
| 99.2 | $7.7 \mathrm{E}-01$ |
| 99.4 | $1.9 \mathrm{E}-01$ |
| 99.0 | $1.7 \mathrm{E}-01$ |
| 96.4 | $7.6 \mathrm{E}-02$ |
| 99.0 | $4.2 \mathrm{E}-01$ |
| 99.2 | $1.4 \mathrm{E}-01$ |
| 98.2 | $4.6 \mathrm{E}-01$ |
| 94.7 | $2.5 \mathrm{E}-01$ |
| 98.9 | $4.0 \mathrm{E}-01$ |
| 99.6 | $4.9 \mathrm{E}-02$ |
| 99.6 | $4.1 \mathrm{E}-01$ |
| 99.5 | $1.4 \mathrm{E}-02$ |
| 95.5 | $5.9 \mathrm{E}-01$ |
| 96.4 | $4.8 \mathrm{E}-01$ |
| 98.3 | $4.7 \mathrm{E}-02$ |


| 0.027 | -0.43 | $4.46 \mathrm{E}-01$ | $1.46 \mathrm{E}-02$ | LOC157273 |
| ---: | ---: | :--- | :--- | :--- |
| 0.027 | 0.82 | $1.54 \mathrm{E}-01$ | $2.70 \mathrm{E}-05$ | FGF20 |
| 0.126 | -0.08 | $7.71 \mathrm{E}-01$ | $9.53 \mathrm{E}-04$ | POP1 |
| 0.084 | -0.87 | $7.37 \mathrm{E}-03$ | $2.39 \mathrm{E}-08$ | UBR 5 |
| 0.400 | -0.10 | $5.79 \mathrm{E}-01$ | $6.51 \mathrm{E}-03$ | LOC101927588 |
| 0.020 | -0.41 | $5.33 \mathrm{E}-01$ | $1.63 \mathrm{E}-03$ | SEMA4D |
| 0.048 | 0.05 | $9.00 \mathrm{E}-01$ | $2.67 \mathrm{E}-03$ | GPAM |
| 0.014 | 0.44 | $5.80 \mathrm{E}-01$ | $2.84 \mathrm{E}-03$ | HSD17B12 |
| 0.030 | -0.54 | $3.15 \mathrm{E}-01$ | $2.02 \mathrm{E}-02$ | FAM111B |
| 0.096 | 0.04 | $9.02 \mathrm{E}-01$ | $1.21 \mathrm{E}-03$ | TENM4 |
| 0.196 | -0.22 | $3.33 \mathrm{E}-01$ | $3.94 \mathrm{E}-04$ | SSCAML1 |
| 0.146 | 0.12 | $6.45 \mathrm{E}-01$ | $3.77 \mathrm{E}-04$ | DCP1B |
| 0.013 | -2.38 | $3.07 \mathrm{E}-03$ | $0.00 \mathrm{E}-16$ | FAN1 |
| 0.265 | 1.30 | $2.09 \mathrm{E}-10$ | $0.00 \mathrm{E}-16$ | MTMR10 |
| 0.193 | 0.49 | $3.23 \mathrm{E}-02$ | $7.97 \mathrm{E}-02$ | SHISA9 |
| 0.364 | 0.27 | $1.58 \mathrm{E}-01$ | $8.11 \mathrm{E}-05$ | USP31 |
| 0.119 | 0.03 | $9.14 \mathrm{E}-01$ | $5.28 \mathrm{E}-04$ | LINC01571 |
| 0.110 | -0.41 | $1.54 \mathrm{E}-01$ | $3.75 \mathrm{E}-02$ | HERPUD1 |
| 0.080 | -0.05 | $8.84 \mathrm{E}-01$ | $3.00 \mathrm{E}-03$ | LINC00470 |
| 0.082 | 0.10 | $7.69 \mathrm{E}-01$ | $4.11 \mathrm{E}-02$ | SLC14A1 |
| 0.053 | -0.22 | $5.99 \mathrm{E}-01$ | $3.97 \mathrm{E}-04$ | PET117 |
| 0.277 | -0.14 | $5.00 \mathrm{E}-01$ | $6.64 \mathrm{E}-02$ | SYNDIG1 |
| 0.206 | -0.33 | $1.56 \mathrm{E}-01$ | $1.44 \mathrm{E}-04$ | LARGE1 |

ither the original standard continuous analysis or extreme dichotomous analysis of the discovery data set. Thus, many

SNPs did not generate strong association signals in the replication data set.

A




