

## Description of Additional Supplementary Files

File Name: Supplementary Data 1

Description: **Meta-EWAS of any CHIP in Black Participants.** A race-stratified meta-EWAS of any CHIP was performed in JHS, CHS, and ARIC. Significance was defined as a Bonferroni-corrected P-value  $< 1 \times 10^{-7}$ , based on two-sided P-values from an inverse variance-weighted fixed-effect meta-analysis.

File Name: Supplementary Data 2

Description: **Meta-EWAS of DNMT3A CHIP in Black Participants.** A race-stratified meta-EWAS of any CHIP was performed in JHS, CHS, and ARIC. Significance was defined as a Bonferroni-corrected P-value  $< 1 \times 10^{-7}$ , based on two-sided P-values from an inverse variance-weighted fixed-effect meta-analysis.

File Name: Supplementary Data 3

Description: **Meta-EWAS of TET2 CHIP in Black Participants.** A race-stratified meta-EWAS of any CHIP was performed in JHS, CHS, and ARIC. Significance was defined as a Bonferroni-corrected P-value  $< 1 \times 10^{-7}$ , based on two-sided P-values from an inverse variance-weighted fixed-effect meta-analysis.

File Name: Supplementary Data 4

Description: **Meta-EWAS of any CHIP in White Participants.** A race-stratified meta-EWAS of any CHIP was performed in FHS, CHS, and ARIC. Significance was defined as a Bonferroni-corrected P-value  $< 1 \times 10^{-7}$ , based on two-sided P-values from an inverse variance-weighted fixed-effect meta-analysis.

File Name: Supplementary Data 5

Description: **Meta-EWAS of DNMT3A CHIP in White Participants.** A race-stratified meta-EWAS of any CHIP was performed in FHS, CHS, and ARIC. Significance was defined as a Bonferroni-corrected P-value  $< 1 \times 10^{-7}$ , based on two-sided P-values from an inverse variance-weighted fixed-effect meta-analysis.

File Name: Supplementary Data 6

Description: **Meta-EWAS of *TET2* CHIP in White Participants.** A race-stratified meta-EWAS of any CHIP was performed in FHS, CHS, and ARIC. Significance was defined as a Bonferroni-corrected P-value  $< 1 \times 10^{-7}$ , based on two-sided P-values from an inverse variance-weighted fixed-effect meta-analysis.

File Name: Supplementary Data 7

Description: **Multiracial Meta-EWAS of any CHIP.** A multi-ancestry meta-EWAS of any CHIP was performed in FHS, JHS, CHS, and ARIC. Significance was defined as a Bonferroni-corrected P-value  $< 1 \times 10^{-7}$ , based on two-sided P-values from an inverse variance-weighted fixed-effect meta-analysis.

File Name: Supplementary Data 8

Description: **Multiracial Meta-EWAS of *DNMT3A* CHIP.** A multiracial meta-EWAS of any CHIP was performed in FHS, JHS, CHS, and ARIC. Significance was defined as a Bonferroni-corrected P-value  $< 1 \times 10^{-7}$ , based on two-sided P-values from an inverse variance-weighted fixed-effect meta-analysis.

File Name: Supplementary Data 9

Description: **Multiracial Meta-EWAS of *TET2* CHIP.** A multiracial meta-EWAS of any CHIP was performed in FHS, JHS, CHS, and ARIC. Significance was defined as a Bonferroni-corrected P-value  $< 1 \times 10^{-7}$ , based on two-sided P-values from an inverse variance-weighted fixed-effect meta-analysis.

File Name: Supplementary Data 10

Description: **EWAS of *ASXL1* CHIP.** A EWAS of *ASXL1* CHIP was performed exclusively in the FHS cohort. Significance was defined as a Bonferroni-corrected P-value  $< 1 \times 10^{-7}$ , based on two-sided P-values from an inverse variance-weighted fixed-effect meta-analysis.

File Name: Supplementary Data 11

Description: **Meta-EWAS Summary Statistics for any CHIP with VAF  $> 10\%$  in Black Participants.** Significance was defined as a Bonferroni-corrected P-value  $< 1 \times 10^{-7}$ , based on two-sided P-values from an inverse variance-weighted fixed-effect meta-analysis.

68 File Name: Supplementary Data 12

69 Description: **Meta-EWAS Summary Statistics for any CHIP with VAF > 10% in White**  
70 **Participants.** Significance was defined as a Bonferroni-corrected P-value  $< 1 \times 10^{-7}$ , based on  
71 two-sided P-values from an inverse variance-weighted fixed-effect meta-analysis.

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73 File Name: Supplementary Data 13

74 Description: **Multiracial Meta-EWAS Summary Statistics for any CHIP with VAF > 10%.**  
75 Significance was defined as a Bonferroni-corrected P-value  $< 1 \times 10^{-7}$ , based on two-sided P-  
76 values from an inverse variance-weighted fixed-effect meta-analysis.

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78 File Name: Supplementary Data 14

79 Description: **Gene Ontology (GO) Enrichment Analysis for Genes Harboring any CHIP-**  
80 **associated CpGs.** The missMethyl R package was used for GO enrichment analysis. Fisher's  
81 Exact Test (one-sided) was used for this analysis.

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83 File Name: Supplementary Data 15

84 Description: **Gene Ontology Enrichment Analysis for Genes Harboring DNMT3A CHIP-**  
85 **associated CpGs.** The missMethyl R package was used for GO enrichment analysis. Fisher's  
86 Exact Test (one-sided) was used for this analysis.

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88 File Name: Supplementary Data 16

89 Description: **Gene Ontology Enrichment Analysis for Genes Harboring TET2 CHIP-**  
90 **associated CpGs.** The missMethyl R package was used for GO enrichment analysis. Fisher's  
91 Exact Test (one-sided) was used for this analysis.

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93 File Name: Supplementary Data 17

94 Description: **Gene Ontology Enrichment Analysis for Genes Harboring ASXL1 CHIP-**  
95 **associated CpGs.** The missMethyl R package was used for GO enrichment analysis. Fisher's  
96 Exact Test (one-sided) was used for this analysis.

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100 File Name: Supplementary Data 18

101 Description: **Any CHIP Expression Quantitative Trait Methylation Loci (eQTMs).** Linear  
102 regression (two-sided) was employed for this analysis.

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104 File Name: Supplementary Data 19

105 Description: ***DNMT3A* CHIP Expression Quantitative Trait Methylation Loci (eQTMs).**  
106 Linear regression (two-sided) was employed for this analysis.

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108 File Name: Supplementary Data 20

109 Description: ***TET2* CHIP Expression Quantitative Trait Methylation Loci (eQTMs).** Linear  
110 regression (two-sided) was employed for this analysis.

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112 File Name: Supplementary Data 21

113 Description: ***ASXL1* CHIP Expression Quantitative Trait Methylation Loci (eQTMs).** Linear  
114 regression (two-sided) was employed for this analysis.

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116 File Name: Supplementary Data 22

117 Description: **Any CHIP Expression Quantitative Trait Methylation Loci (eQTM) Gene  
118 Ontology Enrichment Analysis.** The missMethyl R package was used for GO enrichment  
119 analysis. Fisher's Exact Test (one-sided) was used for this analysis.

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121 File Name: Supplementary Data 23

122 Description: ***DNMT3A* CHIP Expression Quantitative Trait Methylation Loci (eQTM) Gene  
123 Ontology Enrichment Analysis.** The missMethyl R package was used for GO enrichment  
124 analysis. Fisher's Exact Test (one-sided) was used for this analysis.

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126 File Name: Supplementary Data 24

127 Description: ***TET2* CHIP Expression Quantitative Trait Methylation Loci (eQTM) Gene  
128 Ontology Enrichment Analysis.** The missMethyl R package was used for GO enrichment  
129 analysis. Fisher's Exact Test (one-sided) was used for this analysis.

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132 File Name: Supplementary Data 25

133 Description: **ASXL1 CHIP Expression Quantitative Trait Methylation Loci (eQTM) Gene**  
134 **Ontology Enrichment Analysis.** The missMethyl R package was used for GO enrichment  
135 analysis. Fisher's Exact Test (one-sided) was used for this analysis.

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137 File Name: Supplementary Data 26

138 Description: **CpGs Linked to *cis*-mQTLs with GWAS Catalog Traits for any CHIP and**  
139 **CHIP Subtypes.**

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141 File Name: Supplementary Data 27

142 Description: **CpGs Linked to EWAS Catalog Traits for any CHIP and CHIP Subtypes.**  
143 Significance was defined at  $0.05/4023 = 1.24 \times 10^{-5}$ , based on one-sided P-values from an  
144 inverse variance-weighted fixed-effect meta-analysis.

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146 File Name: Supplementary Data 28

147 Description: **Two-Sample Mendelian Randomization.** A two-sample Mendelian  
148 Randomization (MR) analysis was performed.

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150 File Name: Supplementary Data 29

151 Description: **GO Enrichment Analysis for Genes Annotated to TET2-associated CpGs with**  
152 **Decreased Methylation.** The missMethyl R package was used for GO enrichment analysis.  
153 Fisher's Exact Test (over-representation one-sided) was used for this analysis.

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