

Epigenetic editing at individual age-associated CpGs affects the genome-wide epigenetic aging landscape

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Supplemental table S1: Guide RNA sequences for age-associated hyper-CpGs

Target gene and no.	sgRNA-guide sequence	Target CpG ID (Illumina BeadChip)
Hypermethylated with age:		
<i>PDE4C</i> #1	5'-TCTGGCGCATGGAGAACCTG-3'	cg17861230
<i>PDE4C</i> #2	5'-TCGGATCCGGACAAGTCCGC-3'	cg17861230
<i>ELOVL2</i> #1	5'-GACGAAACGGCCCCGAGGCT-3'	cg16867657, cg21572722
<i>ELOVL2</i> #2	5'-GGGGAGAAGCAGTATCGTGC-3'	cg16867657, cg21572722
<i>FHL2</i> #1	5'-GAGAAGCCCCAGGACGTGCCG-3'	cg22454769, cg06639320
<i>FHL2</i> #2	5'-GACTGTGCTCCCAAGACCCGG-3'	cg22454769, cg06639320
<i>KLF14</i> #1	5'-GCAACCCAGAAGTTCCGACTG-3'	cg22285878
<i>KLF14</i> #2	5'-GACGGAGCACGGGATCGGGT-3'	cg22285878
<i>TEAD1</i> #1	5'-GCACAAGTCTGCGCAGACCC-3'	cg04940570
Hypomethylated with age:		
<i>MEIS1-AS3</i> #1	5'-CAAGTGAATAACTACTCAGC-3'	cg11807280
<i>COL1A1</i> #1	5'-TAAGATTGGAGAAGGTTGAC-3'	cg18618815
<i>COL1A1</i> #2	5'-TCTCCTATAGAAGAACTCCC-3'	cg18618815
<i>AKAP8L</i> #1	5'-CACACGTGTTAAGTACTCTT-3'	cg25533247
<i>CSNK1D</i> #1	5'-GCCTTACCTCCTGACACCTA-3'	cg19761273
<i>IGSF11</i> #1	5'-TAATCAATAAGACCTTCCTA -3'	cg00329615
<i>IGSF11</i> #2	5'-GGCTACGATTCAGGGACACC-3'	cg00329615

Supplemental table S2: Primers for pyrosequencing

Gene name	Label	Primer sequence
<i>PDE4C</i>	Forward	5'-AGGTTTGTAGTAGGTTGAG-3';
	Reverse	Biotin-5'-AACTCAAATCCCTCTC-3'
	Seq-Primer	5'-GTTATAGTATGATTAGAGTTT-3'
<i>FHL2</i>	Forward	5'-GTGTTTTTTAGGGTTTTGGGAGTATAGTAGT-3'
	Reverse	Biotin-5'-CACCTCCTAAACTTCTCCAATCTCC-3'
	Seq-Primer	5'-GGTTTTGGGAGTATAGTAGTT-3'
<i>ELOVL2</i>	Forward	5'-Biotin-GGGAGGGGAGTAGGGTAAGTGA-3'
	Reverse	5'-CCATCTAAACAACCAATAAATATTCCTAAA-3'
	Seq-Primer	5'-AATAAATATTCCTAAACTC-3'
<i>MEIS1-AS3</i>	Forward	5'-ATTTTTGTTTGAAGGTTTTTATAAAATATG-3'
	Reverse	5'-ACCTTTAAAACAACAAAATAAATCACACT-3'
	Seq-Primer	5'-ACCATACTTAACATCCA-3'
<i>AKAP8L</i>	Forward	5'-TGAAGTTTGGAATTTATGATTTGTTTAAG-3'
	Reverse	Biotin-5'-CCCAAAAAACAACTAAAAACATAACTAAT-3'
	Seq-Primer	5'-GAGAGATTTTGTAAATAGTGTA-3'
<i>CSNK1D</i>	Forward	5'-GGAGGTTTTGATGTTTAGTTTGAAGAT-3'
	Reverse	Biotin-5'-CAAATCCAACACAAATAAAAATATTAAGTC-3'
	Seq-Primer	5'-GGTTAGATTATTTGTTTTTTTTTAG-3'
<i>COL1A1</i>	Forward	5'-TTGAAGGGAAGAGGTAAGGAAGATTTTA-3'
	Reverse	Biotin-5'-TAACCCATCTTTTCTTCTTCTCA-3'
	Seq-Primer	5'-AATTTGTATAGAGAGTGTTTATTG-3'
<i>IGSF11</i>	Forward	5'-GTTGGATAGTTTGTGGGTAGAAAATTTA-3'
	Reverse	Biotin-5'-ATTATTCATTCAATTCTCCTTAAAAAATCTTATT-3'
	Seq-Primer	5'-AGAAGTTAAGAAGGTATAGATA-3'

Supplemental table S3: Primers for bisulfite amplicon sequencing

Gene Name	Label	Primer sequence
PDE4C, 1st PCR	Forward	5'-CTCTTTCCTACACGACGCTCTTCCGATCTTATGGAGAATTT GGGG-3'
	Reverse	5'-CTGGAGTTCAGACGTGTGCTCTTCCGATCTCTACAAAAAC CCCTACC-3'
Adapters, 2nd PCR	i5	5'-AATGATACGGCGACCAACCGAGATCTACACTCTTTCCTACAC GACGCTCTTCCGATCT-3'
	i7	5'-AGATCGGAAGAGCACACGTCTGAACTCCAGTCAC[Barcode]AT CTCGTATGCCGTCTTCTGCTTG-3'

Supplemental table S4: Primers for i4C sequencing

Primer	Location (hg38)	Adapter primer Illumina; view-point specific sequence
Pri-PDE4C-NlaIII	chr19:18233097-18233114	5'-TCGTCGGCAGCGTCAGATGTGTATAAGAGACAG-3'; 5'-AGGTGCTTCGGGGCTCTG-3';
Sec-PDE4C_CviQI	chr19:18232652-18232672	5'-GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAG-3'; 5'-CCAGATGTGTTTGGGGTGCTC-3'
Pri-FHL2-NlaIII	chr2:105399436-105399455	5'-TCGTCGGCAGCGTCAGATGTGTATAAGAGACAG-3'; 5'-AGGGGGTCACTTCTCAGGAG-3'
Sec-FHL2_CviQI	chr2:105399228-105399247	5'-GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAG-3'; 5'-AAGAAAGGAGCCCTGGCAA-3'
Pri-MEIS1-ApoI	chr2:66427399-66427383	5'-TCGTCGGCAGCGTCAGATGTGTATAAGAGACAG-3'; 5'-GAAGGCTTCCTGCGGCG-3'
Sec-MEIS1_CviQI	chr2:66427579-66427598	5'-GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAG-3'; 5'-AGTGACTAGAGCACGTTTCGC-3'