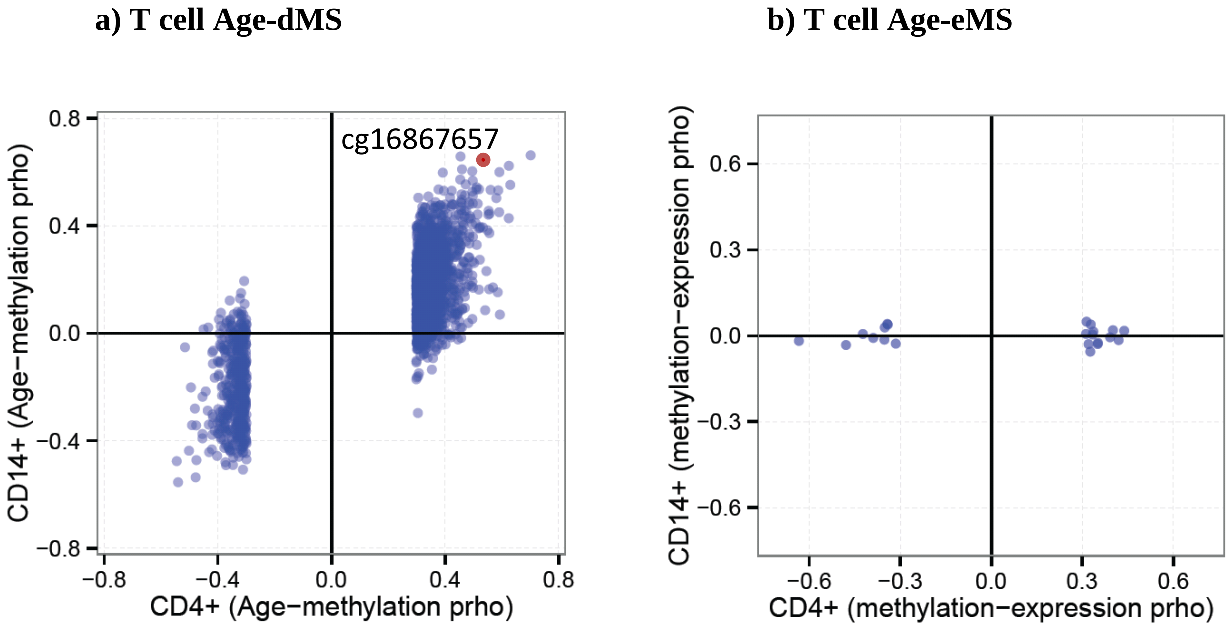
Supplementary Information



a) T cell Age-dMS

b) T cell Age-eMS

Supplementary Figure 1 | Replication of T cell Age-dMS and Age-eMS in 1,264 monocyte samples. Analysis of age and methylation in 227 T cell (CD4+) samples included 436,393 CpG methylation sites, of which 2,595 had methylation associated with age (age-dMS; FDR<0.001): 546 negatively associated with age (hypo age-dMS), 2,049 positively associated with age (hyper age-dMS); see **Supplementary Table 2**. **a)** Comparison of the partial correlation (prho) between methylation and age in 227 T cell samples (x-axis) compared to the correlation detected in 1,264 monocyte samples (CD14+, y-axis). The most significant T cell age-dMS (red circle, cg16867657, prho = 0.70, FDR = 6.72×10^{-28}) was detected on chromosome 6 in the *ELOVL2* (ELOVL fatty acid elongase 2) promoter. **b)** Comparison of the correlation between methylation and *cis*-gene expression for age-dMS associated with *cis*-gene expression in 227 T cells (22 CD4+ age-eMS, FDR<0.001, x-axis; restricted to age-dMS detected in both monocytes and T cells FDR<0.001), compared to the correlation in 1,264 monocyte samples (y-axis). Linear regression analysis also included the following covariates: race, sex, site of data collection, and residual sample contamination with non-targeted cells (see **Methods**).

Supplementary Table 1 | Population characteristics for all participants included in analysis (and by race)

Variable	**All (n = 1,264)**	**Caucasian (n = 590)**	**Hispanic (n = 402)**	**African-American (n = 272)**
Age (years)	60 ±10	60 ± 10	59 ± 9	61 ± 9
Women	650 (51%)	285 (48%)	202 (50%)	163 (60%)
Former smoker	358 (50%)	183 (53%)	104 (49%)	71 (44%)
Current smoker	69 (10%)	31 (9%)	18 (8%)	20 (12%)
Pulse pressure (mmHg)	58 ± 18	56 ± 17	57 ± 18	62 ± 18
BMI (kg/m^2)	30 ± 6	29 ± 5	30 ± 5	31 ± 6
Hypertension	596 (61%)	278 (55%)	163 (58%)	155 (78%)
Diabetic	289 (23%)	81 (14%)	106 (26%)	102 (38%)

Mean ± standard deviation provided for continuous variables; count (percentage) provided for discrete variables

Supplementary Table 2 | Association of major histocompatibility complex (MHC) class I and II mRNA expression transcripts with age

a) MHC class I

Gene	Illumina probe ID	Chr	Age beta	SE	P value	FDR
TAP2	**ILMN_1777565**	**6**	**0.0057**	**0.0012**	**3.64E-06**	**2.00E-05**
TAPBP	**ILMN_1742450**	**6**	**0.0031**	**0.0008**	**1.28E-04**	**3.09E-04**
TAPBP	**ILMN_1782851**	**6**	**0.0045**	**0.0012**	**2.59E-04**	**5.42E-04**
HLA-E	**ILMN_1765258**	**6**	**0.0018**	**0.0006**	**3.78E-03**	**4.87E-03**
HLA-B	**ILMN_1778401**	**6**	**0.0013**	**0.0006**	**0.02**	**0.02**
TAP2	**ILMN_1759250**	**6**	**0.0027**	**0.0013**	**0.04**	**0.03**
HLA-C	ILMN_1721113	6	0.0049	0.0030	0.11	0.07
MICB	ILMN_1708006	6	0.0009	0.0007	0.21	0.12
HLA-F	ILMN_1762861	6	0.0008	0.0008	0.36	0.18
MICA	ILMN_1797929	6	0.0010	0.0013	0.46	0.21
HLA-F	ILMN_2186806	6	0.0006	0.0009	0.48	0.22
HLA-A	ILMN_1671054	6	-0.0007	0.0012	0.56	0.24
HLA-C	ILMN_2150787	6	0.0006	0.0059	0.92	0.34
HLA-G	ILMN_1656670	6	-0.00004	0.0010	0.97	0.35

b) MHC class II

Gene	Illumina probe ID	Chr	Age beta	SE	P value	FDR
CD74	**ILMN_1761464**	**5**	**0.0060**	**0.0012**	**2.39E-07**	**2.54E-06**
HLA-DPA1	**ILMN_1772218**	**6**	**0.0041**	**0.0008**	**4.12E-07**	**3.90E-06**
CD74	**ILMN_2379644**	**5**	**0.0039**	**0.0008**	**1.10E-06**	**8.11E-06**
CD74	**ILMN_1736567**	**5**	**0.0036**	**0.0007**	**1.17E-06**	**8.41E-06**
HLA-DMA	**ILMN_1695311**	**6**	**0.0024**	**0.0007**	**3.04E-04**	**6.19E-04**
HLA-DOA	**ILMN_1659075**	**6**	**0.0048**	**0.0017**	**5.09E-03**	**6.18E-03**
HLA-DRB3	**ILMN_1717261**	**6**	**0.0035**	**0.0016**	**0.03**	**0.03**
HLA-DPB1	**ILMN_1749070**	**6**	**0.0028**	**0.0016**	**0.07**	**0.05**
HLA-DRB4	ILMN_1752592	6	0.0024	0.0014	0.09	0.06
HLA-DQB1	ILMN_1661266	6	0.0057	0.0041	0.16	0.10
IFI30	ILMN_1807277	19	0.0005	0.0007	0.48	0.22
HLA-DOB	ILMN_1700428	6	-0.0008	0.0012	0.49	0.22
HLA-DRB4	ILMN_2159694	6	-0.0052	0.0075	0.49	0.22
HLA-DRB5	ILMN_1697499	6	-0.0062	0.0093	0.50	0.23
HLA-DMB	ILMN_1761733	6	-0.0004	0.0006	0.51	0.23
HLA-DQA1	ILMN_1808405	6	0.0012	0.0030	0.69	0.28
HLA-DRB1	ILMN_1715169	6	-0.0033	0.0087	0.71	0.29

Effect size (Age beta), standard error (SE), and significance (P-value and FDR) for the associations of age with expression of 24 genes (31 mRNA expression transcripts (Illumina probe ID)) annotated as major histocompatibility complex (MHC) class I (n = 10) or class II genes (n = 14) in Pubmed; All age-associated (FDR ≤ 0.05) MHC genes have increasing expression associated with age (shown in bold; 10 genes; 14 mRNA expression transcripts) in 1,264 CD14+ monocyte samples