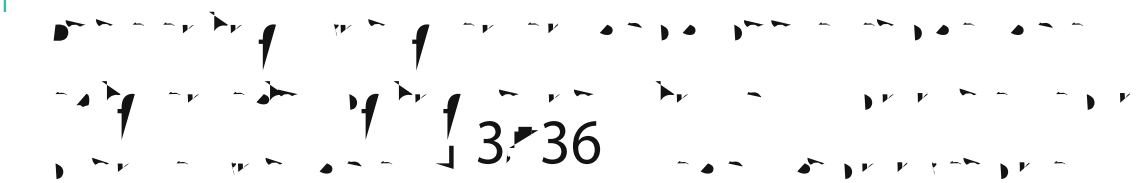
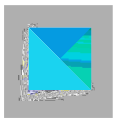
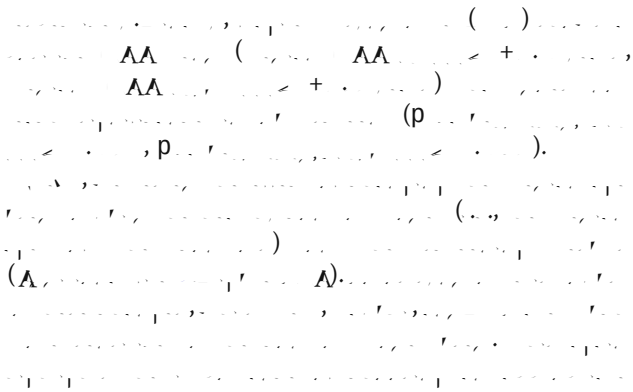






( ),

(p , A,).

(, p ,).

NSD1

Discussion

epigenetic clock theory of aging,

noob

(DNAmAge)

Conclusions

epigenetic maintenance system

Methods

Sample collection and annotation

Pre-processing, QC, and filtering the data for the epigenetic clock calculations

minfi

noob

epidish

EpiDISH

Calculating the epigenetic age acceleration and performing the main screen

control models)

(I) Without cell composition correction (CCC):

(II) With cell composition correction (CCC):

DNAmAge

Age, PCN

N

Gran, CD4T, CD8T, B, Mono, NK

lm

(III) MAE = median((EAA))

(DNAmAge)

( ).

Identifying differentially methylated positions

dmpFinder minfi [' ( )
BMC)mean]. (– , N)
(p
Age)

(VII) β ~Age + Sex + Gran + CD4T + CD8T + B + Mono + NK + PC1 + ... + PC17

β_i
i ( ) .

(N) (N)
( ) [
(p
Disease_status)

(VIII) β ~Disease _ status + Age + Sex + Gran + CD4T + CD8T + B + Mono + NK + PC1 + ... + PC17

α . .

(Epi) genomic annotation of the CpG sites

( )
. A
hg19 .

pyBigWig [.
[.
( )

– ChIP-seq data from ENCODE (histone modifications from peripheral blood mononuclear cells or PBMC; EZH2, as a marker of polycomb repressing complex 2 binding, from B cells; RNF2, as a marker of polycomb repressing complex 1 binding, from the K562 cell line). We obtained - scores (using the function in R) for the values of "fold change over control" as calculated in ENCODE [96]. When needed, biological replicates of the same feature were aggregated by taking the mean of the -scores in order to obtain the
[redacted]
quantified as "normalised read counts" or NRC) and Repli-seq data for replication timing (GSM923447, quantified as "wavelet-transformed signals" or WTS). We used the same data from the IMR90 cell line as in [97].
– Total RNA-seq data (rRNA depleted, from PBMC) from ENCODE. We calculate

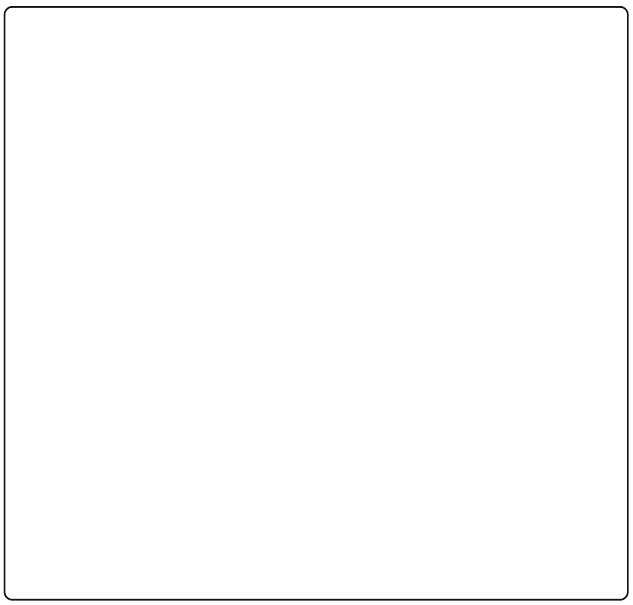
Differences in the clock CpGs beta values for Sotos syndrome

(control CpG models,

(X) $\beta \sim Age + Age^2 + Sex + Gran + CD4T + CD8T + B + Mono + NK + PC1 + ... + PC17$

β_i

i



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