

Meta-analysis of DNA methylation aging signatures in 17 human tissues

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Meta Analysis of DNA Methylation Aging Signatures in 17 Human Tissues

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SUPPLEMENTARY DATA

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Supplementary Figures:

Figure 1 Overview of the analytical framework applied in this study

Supplementary Tables:

Table 1 Summary of datasets included in the studies and models used for each dataset.

Table 2 Global Methylation analysis results

Table 3 DMPs and VMPs before and after cell-type correction

Table 4 Power calculation results

Table 5 Permutation-based sensitivity analysis for the overlap likelihood of VMPs and DMPs.

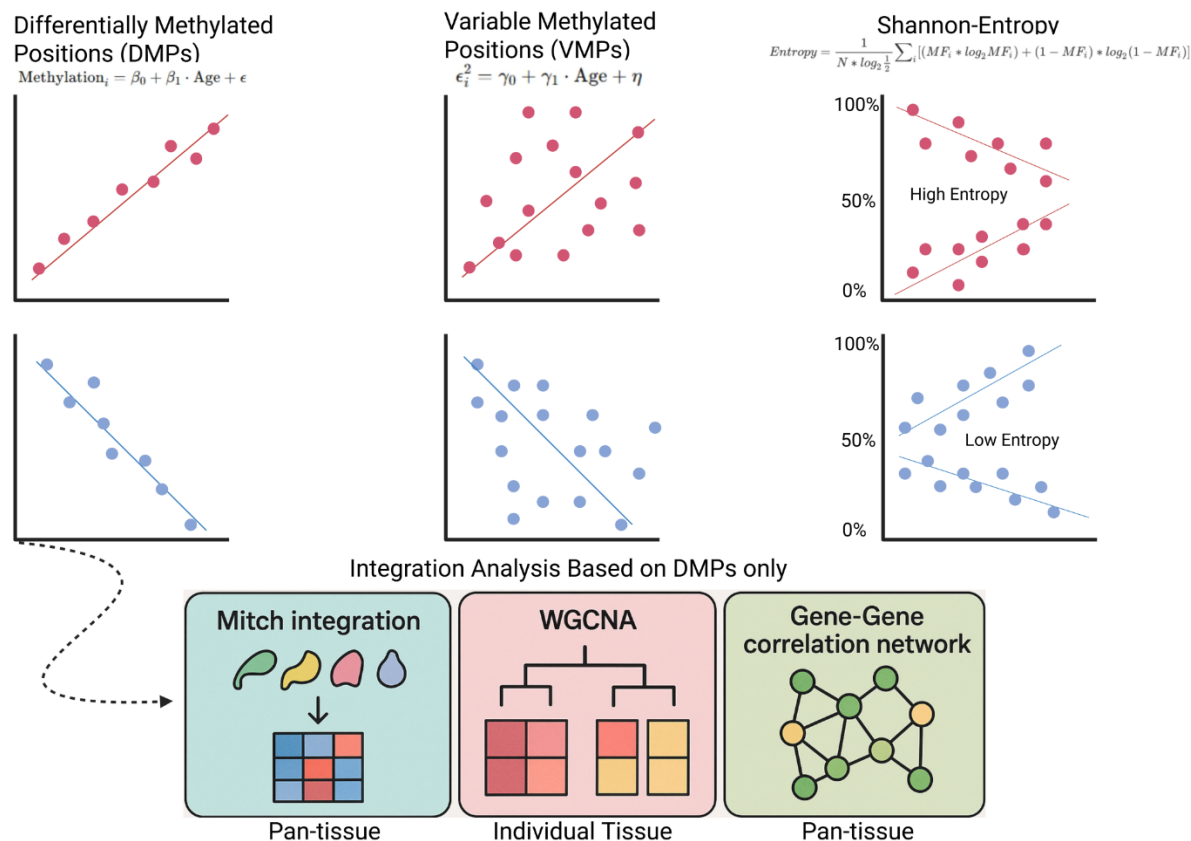
Table 6 Pan-tissue analysis of gene-gene networks

Table 7 In-silico perturbation analysis findings featuring key contributing genes and pathways

Table 8 Transitions in CpG methylation states between younger (≤ 30 years) and older (≥ 60 years) individuals across tissues. CpGs are categorized as low (< 0.25), intermediate ($0.25 - 0.75$), or high (> 0.75), and values represent the number (or proportion) shifting between states with age. Transitions toward intermediate methylation (low $\rightarrow$ intermediate; high $\rightarrow$ intermediate) are consistent with stochastic/entropic drift, whereas maintenance within or shifts reinforcing extreme states may reflect more structured remodeling. Interpretation should be made alongside direction-of-change results (Fig 4), as apparent hypermethylation can arise from drift toward intermediate states when baseline methylation is predominantly low.

Table 9 Top pan-tissue DMPs present in 13 or more tissues.

Supplementary Figures



Supplementary Figure 1 Overview of the analytical framework applied in this study.

Illustration of the three methylation metrics used to characterise age-associated epigenetic changes across tissues. Differentially methylated positions (DMPs) are identified using a linear regression model, capturing directional shifts in mean methylation level with age; red dots and regression line indicate hypermethylation with age and blue dots and regression line indicate hypomethylation with age. Variably methylated positions (VMPs) are identified using a heteroscedasticity-based framework, detecting age-associated increases in inter-individual variance in methylation; red and blue indicate increasing and decreasing variance with age respectively. Shannon entropy is calculated per sample using the formula shown, quantifying genome-wide methylation disorder; high entropy (red) reflects methylation values converging toward 50%, indicating maximum uncertainty, while low entropy (blue) reflects methylation values approaching 0% or 100%. The lower panel illustrates the three downstream integration analyses applied to DMP-level results: match integration, a pan-tissue multivariate pathway enrichment approach combining gene-level t-statistics across tissues into a gene $\times$ tissue matrix; Weighted Gene Co-expression Network Analysis (WGCNA), applied at the individual tissue level to identify co-methylation modules; and gene-gene correlation network analysis, a pan-tissue approach constructing pairwise Spearman correlation matrices from tissue-level t-statistics to identify genes with coordinated aging trajectories across organs.

