

Extended Figure S1. Flowchart for inclusion of participants from the Massachusetts General Brigham (MGB) Biobank for the development of *EMRAge*.



Extended Figure S2. Pearson's correlation between *EMRAge* and chronological age in the test and train sets.





Extended Figure S3. Distribution of super pathways (A) and subpathways for all the metabolites (B).

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EMRAge	***	***	***	***	*	**		**	*		***		•	**	•		0.8
DNAm EMRAge	***	***	***	***	*	**		**	*		***			***		-	0.6
PCHorvath Pan tissue	***	**	**	***	*	*		**	*		***			**			
PCHorvath Skin&Blood	***	**	**	***	*	*		**	*		***			**			0.4
PCHannum	***	**	**	***	*	*		**	*		***			**		-	0.2
PCPhenoAge	***	**	**	***	**	**		**	*		***			***			
PCDNAmTL	••••	**	**	***		*		**	٠		***			**			U
PCGrimAge	•••	***	***	***	*	*		**	*		***			**			-0.2
Horvath	***	**	**	***		*		*	*		***			*			-0.4
Hannum	***	**	**	***	*	*		**	*		***			**			
PhenoAge	***	**	**	***	*	*		**	*		***			**			-0.6
DunedinPACE	***	*	*	***	***	***	*	***	***		***	*	**	***			-0.8
OMICm Age	***	***	***	***	*	*		**	*		***	•	•	**			-1

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Extended Figure S4. Correlation plots between epigenetic clocks and immune cells in the MGB-ABC and TruDiagnostic biobanks. A) Discovery cohort - MGB-ABC biobank. B) Validation cohort - TruDiagnostic biobank. Each column represents a covariate among age, gender male, gender female, and immune cells. The size is related to the magnitude of the correlation and the color to the direction (positive or negative). *: p-value < 0.05, **: p-value < 0.01, ***: p-value < 0.001.