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The PedBE clock accurately estimates DNA methylation age in pediatric buccal cells.

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Abstract

The development of biological markers of aging has primarily focused on adult samples. Epigenetic clocks are a promising tool for measuring biological age that show impressive accuracy across most tissues and age ranges. In adults, deviations from the DNA methylation (DNAm) age prediction are correlated with several age-related phenotypes, such as mortality and frailty. In children, however, fewer such associations have been made, possibly because DNAm changes are more dynamic in pediatric populations as compared to adults. To address this gap, we aimed to develop a highly accurate, noninvasive, biological measure of age specific to pediatric samples using buccal epithelial cell DNAm. Wegathered 1,721 genome-wide DNAm profiles from 11 different cohorts of typically developing individuals aged 0 to 20 y old. Elastic net penalized regression was used to select 94 CpG sites from a training dataset (n = 1,032), with performance assessed in a separate test dataset (n = 689). DNAm at these 94 CpG sites was highly predictive of age in the test cohort (median absolute error = 0.35 y). The Pediatric-Buccal-Epigenetic (PedBE) clock was characterized in additional cohorts, showcasing the accuracy in longitudinal data, the performance in nonbuccal tissues and adult age ranges, and the association with obstetric outcomes. The PedBE tool for measuring biological age in children might help in understanding the environmental and contextual factors that shape the DNA methylome during child development, and how it, in turn, might relate to child health and disease.

Keywords: DNA methylation, Age, Development, Epigenetic clock, Adolescence