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Title: ATAC-CLOCK: AN AGING CLOCK BASED ON CHROMATIN ACCESSIBILITY

Abstract: The establishment of aging clocks highlighted the strong link between changes in DNA methylation and aging. Yet, it is still unknown if other epigenetic features could be used to predict age accurately. In this study, we collected blood from 159 human donors and generated chromatin accessibility, transcriptomic, and cell composition data. We investigated how chromatin accessibility changes during aging and constructed a novel aging clock with a median absolute error of 5.27 years. The changes in chromatin accessibility used by the clock were strongly related to transcriptomic alterations, aiding clock interpretation. We additionally show that our chromatin accessibility clock performs significantly better than a transcriptomic clock trained on matched samples. Finally, we demonstrate that the clock relies on cell-intrinsic chromatin accessibility alterations rather than changes in cell composition. Thus, we provide a new method to generate accurate and interpretable aging clocks.