# Title: Prospective association of circulating inflammatory biomarkers with epigenetic ageing in the Young Finns Study

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## Abstract
DNA methylation-based epigenetic clocks have been established as reliable measures of biological age and aging rate. Chronic inflammation is a potential contributor to aging and various diseases; however, population-based prospective studies exploring the impact of specific inflammatory biomarkers on epigenetic clocks remain limited.

This study aims to investigate the prospective associations between 38 specific inflammatory biomarkers, as well as a combined systemic inflammation variable, and epigenetic clocks within a middle-aged population.

The study cohort comprised 1,327 middle-aged Finnish participants (aged 30–45 years, 50–55% female) from the longitudinal Young Finns Study. The prospective associations between 38 inflammatory serum biomarkers—measured during the 2007 follow-up—and epigenetic clocks—measured during the 2011 and 2018 follow-ups—were analyzed. DunedinPACE and PCGrimAgeDev epigenetic clocks were calculated using corresponding algorithms derived from genome-wide blood methylation data. These clocks served as endpoints in three multiple linear regression models adjusted for covariates, including age, sex, BMI, smoking, socioeconomic status, alcohol consumption, and physical activity.

Out of the 38 inflammatory biomarkers studied, 11 showed positive associations with DunedinPACE across both follow-ups. Seven biomarkers demonstrated positive associations with PCGrimAgeDev in the 4-year follow-up, although no statistically significant associations were observed in the 11-year follow-up. In both follow-ups, the combined systemic inflammation marker was positively associated with both epigenetic clocks.

This study advances current understanding by providing robust evidence that specific circulating inflammatory biomarkers are positively associated with epigenetic clocks both cross-sectionally and longitudinally. Collectively, these findings suggest that pro-inflammatory cytokines may contribute to biological aging.