

Name: Min-Ae Song

Email: Song.991@osu.edu

Epigenetic Aging in the Human Lung: Focus on Smoking and Vaping

Kellie M. Mori¹, Jo L. Freudenheim², Joseph P. McElroy³, Daniel Y. Weng³, Sarah A. Reisinger³,
Mark D. Wewers⁴, Peter G. Shields², Min-Ae Song¹

¹Division of Environmental Health Sciences, College of Public Health, The Ohio State University, Columbus, OH; ²Department of Epidemiology and Environmental Health; School of Public Health and Health Professions; University at Buffalo; Buffalo, NY; ³Comprehensive Cancer Center, The Ohio State University and James Cancer Hospital, Columbus, OH;

⁴Pulmonary and Critical Care Medicine, Department of Internal Medicine, The Ohio State University, Columbus, OH

Aging lung and cigarette smoking are the main risk factors for pulmonary diseases. Sever epigenetic aging estimates by DNA methylation (mAge) and their acceleration (mAge-Accel) are associated with smoking and lung diseases, mostly in blood. No study has evaluated target organ effects of smoking and vaping on mAge and its impact on lung inflammation and expression in healthy individuals.

Lung mAge was assessed in electronic-cigarette vapers (EC, n=14), smokers (SM), (n=16), and non-EC/non-SM (NS, n=39). We investigated associations of mAge estimators with chronological age (DNAmAge), lifespan (GrimAge), and telomere length (DNAmTL) between groups using linear regression controlling for chronological age and gender (FDR<0.1). mAge-Accel was associated with smoking/EC history, urinary biomarkers, lung cytokines, and transcriptome using Spearman or partial correlations adjusting for chronological age and gender.

EC and SM had significantly older GrimAge and shorter DNAmTL, as well as significantly accelerated GrimAge and decelerated DNAmTL compared to NS. SM only had significantly positive associations of GrimAge-Accel with cotinine and smoking-related markers such as 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) and cigarettes per day. Smoking-related cytokines (IL-1 β , IL-6, and IL-8) and 759 transcripts were significantly associated with GrimAge-Accel. GrimAge-Accel-associated genes were highly enriched in immune-related pathways and play in the morphology and structures of cells/tissues.

Faster lung mAge for SM is consistent with prior studies, and faster lung mAge for EC compared to NS is the first to demonstrate possible effects of EC on biological aging. Our findings suggest that mAge may provide additional insight into heath and pulmonary diseases related to smoking and vaping.