Salivary microRNAs reveal age-associated patterns in healthy adults: an exposome-integrated analysis from the One-Health Aging Project

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Aging is a heterogeneous biological process shaped by interactions between intrinsic molecular mechanisms and lifetime environmental exposures. In an era where increasing lifespan fails to match healthspan extension, there is an urgent need for biomarkers to monitor age-related physiological decline and guide exposome- and lifestyle-based interventions. Circulating microRNAs (miRNAs) represent promising biomarkers of aging due to their regulatory roles and stability in peripheral biofluids; however, their integration into exposome frameworks in healthy populations remains poorly understood.

Within the project 'Integrated innovative technologies for the development of a One-Health approach in the elderly population (One-Health Aging)', we evaluated the salivary expression of seven circulating miRNAs in 131 volunteers aged 40 and over, integrating molecular data with demographic, functional, and exposome-related variables derived from a lifestyle quality questionnaire.

A multistep analytical framework revealed negative associations between age and six out of the seven analyzed salivary miRNAs, alongside strong inter-miRNA correlations indicating a coordinated internal molecular structure of the panel. This was further supported by miRNA-based principal component analysis (PCA), which identified a dominant molecular axis (PC1), explaining 56.3% of the total variance and capturing a shared age-linked miRNA signature. Consequently, to explore potential molecular stratification, unsupervised clustering algorithms were applied to the principal component space. The resulting molecular subgroups were then characterized to reveal lifestyle and environmental differences.

Overall, these findings suggest the existence of a coordinated salivary miRNA signature associated with aging in healthy individuals. Detectable through a non-invasive approach, it offers potential for further refinement and validation within a One Health context, linking molecular regulation to environmental influences for precision prevention and lifestyle-targeted intervention.