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Abstract

Blood Surrogate Epigenetic Biomarkers of Atherosclerosis Reveal Common Signature of Inflamm-Aging-Disorders †

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Abstract: DNA methylation is the most well-known epigenetic modification of DNA. This epigenetic mark is crucial in controlling gene expression profiles, maintaining cellular identity, genomic imprinting and X-chromosome inactivation. Furthermore, DNA methylation is plastic and can adapt to environmental stimuli, acting as a cellular memory of past events. Whereas epigenetic DNA methylation profiling in cancer diagnostics is now well established, associations with other chronic age-associated diseases, including obesity, diabetes, cardiovascular and neurological diseases have recently started to be explored for prognostic, diagnostic and therapeutic applications. Upon genome-wide DNA methylation profiling of whole blood samples from atherosclerotic patients, we characterized various atherosclerosis specific differentially methylated regions (DMRs). Interestingly, similar DMRs were also observed in other age-and inflammation-associated diseases, like obesity, cancer, Alzheimer's and Parkinson's disease, both in blood as well as in brain and tumor tissues. This suggests that inflammaging diseases share a common epigenetic signature of the immune system, which is different from the classic epigenetic clock signature. Furthermore, a cardio-protective flavanol-rich diet intervention can partially reverse this inflammaging disease associated epigenetic pattern. We found that this methylation profile mainly reflects shifts in immune cell type composition and infiltrating immune cell populations. Upon correcting for differences in immune cell composition in blood samples, we identified BRCA1 DNA methylation as an atherosclerosis-specific methylation biomarker irrespective of variations in immune cell biomarkers. How BRCA1 DNA methylation differentially promotes cancer, neurodegeneration or atherosclerosis pathologies requires further investigation. In conclusion, atherosclerosis patient blood samples reveal inflammaging and atherosclerosis-specific DNA methylation biomarkers, which could potentially be used as lifestyle biomarkers to estimate disease risk of neurodegeneration, cardiometabolic disorders and cancer in aging populations.

Keywords: epigenetic biomarker; atherosclerosis; inflammaging

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