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MULTI-OMICS DISSECTION OF TRANSCRIPTIONAL AND EPIGENETIC REMODELING DURING CARDIAC AGING

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Aging is a dominant risk factor for cardiovascular diseases (CVDs), the leading cause of death worldwide. This is reflected in a markedly higher prevalence of heart and circulatory conditions in individuals over 65 years of age [1]. A major contributor to the age-dependent decline in cardiac function is the extensive structural and functional remodeling of the myocardium, which involves all major cardiac cell types. Such remodeling results in cardiomyocyte hypertrophy, vascular stiffening, systolic and diastolic function deterioration, as well as profound metabolic and electrical dysfunctions [2,3]. Nevertheless, the molecular mechanisms underlying these age-associated changes remain largely unknown.

To address this gap, we sought to investigate epigenetic landscapes across multiple cardiac cell types to better decipher how regulatory networks and cell population dynamics shape cardiac aging. This was achieved by an integrative single-nucleus multi-omic approach to simultaneously characterize chromatin accessibility (snATAC-seq) and gene expression (snRNA-seq) profiles of mouse cardiac tissue at 2, 6, 18, 24 months of age. Overall, this study provides valuable insight into the dynamic and cell type-specific epigenetic and transcriptional reprogramming of the aging heart. By leveraging multi-omic profiles across the lifespan, we reveal how such reprogramming contributes to the progressive decline in cardiac function. These findings not only advance our molecular understanding of the aging process but also highlight potential regulatory elements and pathways that may be targeted for therapeutic intervention.

References

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