

Deciphering The Epigenetic Clock: Molecular Mechanism of Ageing and Rejuvenation

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Structured Abstract

Background: The concept of the epigenetic clock has gained significant interest in the field of ageing research and holds potential for cell rejuvenation. Unlike chronological age, which merely reflects years since birth, epigenetic clocks function as biomarkers of biological ageing. They estimate an individual's true physiological condition by analysing DNA methylation (DNAm) patterns. This biological age is considered a more accurate indicator of overall health and can predict the risk of various age-related diseases and mortality. The phenomenon of Epigenetic Age Acceleration (AgeAccel), where biological age surpasses chronological age, is often associated with a higher risk of age-related health issues and mortality. Understanding these clocks is crucial for advancing biomedical knowledge and potentially developing strategies to delay or reverse the ageing process.

Literature Review: Ageing is characterized by several hallmarks, and epigenetic alterations, including DNAm, histone modifications, chromatin remodelling, and RNA modification, significantly influence gene expression in this process. DNAm is highlighted as the main biological process affecting the epigenetic clock, with age-related changes notably involving promoter-specific hypermethylation and genome-wide hypomethylation. This study distinguishes between First-Generation epigenetic clocks such as Horvath and Hannum, primarily predicting chronological age, and Second-Generation clocks such as PhenoAge and GrimAge. GrimAge is identified as the most predictive for morbidity and mortality, integrating lifestyle indicators and plasma protein biomarkers. The rate of epigenetic ageing is influenced by genetic factors but significantly driven by lifestyle and environmental exposures. Caloric Restriction and physical activity can slow epigenetic ageing, while factors like alcohol consumption, smoking, air pollution, extreme heat, chronic inflammation, and metabolic disorders (e.g., obesity, type 2 diabetes) accelerate it. To counter ageing, various rejuvenation strategies are explored. These include Heterochronic Parabiosis, demonstrating the rejuvenating effects of a young systemic environment, Metabolic Manipulation/Dietary Interventions that influence nutrient-sensing pathways and epigenomic remodelling, Senescent Cell Ablation through genetic approaches or senolytic drugs, and Cellular Reprogramming.

Conclusion: Epigenetic clocks estimate biological age via DNAm patterns, with their rate influenced by genetic, lifestyle, environmental, and health factors. This understanding supports rejuvenation strategies that actively aim to restore youthful states, promising improved longevity and vitality.

Keywords: Epigenetic Clock, Ageing, DNA Methylation, Biological Age, Rejuvenation

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