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Epigenetics and human aging

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Epigenetic changes are critical in regulating development and differentiation. Aging may also be an epigenetically driven process. For example, several recent articles describe specific DNA methylation changes as human aging biomarkers. Prominent among these is the "epigenetic aging clock" developed by Dr. Steve Horvath based on Illumina array data. The Horvath clock uses a weighted average of methylation status at 353 CpGs to estimate biological age. This method has been found to apply to both sorted cell types (e.g. neurons, glial cells, monocytes, T-cells) as well as complex tissues (e.g. blood, brain, lung, kidney, bone). It is not yet known whether the epigenetic clock applies to urine sample in a similar manner. Urine is an attractive sample type because of the non-invasive method needed for collection and its composition of several cell types. However, DNA in urine is prone to degradation. Conventional urine storage (i.e. sample freezing and additives) have limited positive impacts on nucleic acid quality. Therefore, we developed a well-standardized procedure of urine sample collection, storage, and nucleic acid purification. Using this robust procedure, we evaluated the accuracy of the epigenetic clock method in human urine samples (n=70) from subjects with an age range from 2 to 84 years. DNA methylation age was highly correlated with chronological age (cor=0.95, p=4.3e-36), demonstrating that the epigenetic clock applies to human urine samples. We have also developed a multiplex NGS-based platform for epigenetic aging prediction. This novel platform is both less expensive and more flexible than the array-based method, allowing integration of customer-designed sites. The combination of this NGS-based platform and non-invasive sampling will allow broad use of the Epigenetic Aging Clock in academic/clinical, forensic and direct-to-consumer markets. We also anticipate wide use of this combination to assess aging/anti-aging effects of disease states, drugs or lifestyle changes.

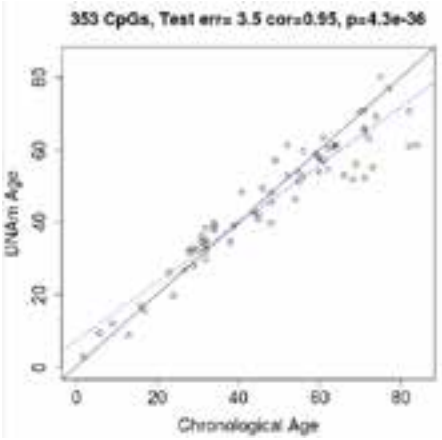

Figure 1: Predicted epigenetic age of urine samples from healthy donors. N=70, 353 CpGs, Test err=3.5, cor=0.95, p=4.3e-36.

Recent Publications

1. Horvath S (2013) DNA methylation age of human tissues and cell types. Genome Biology doi:10.1186/gb-2013-14-10-r115.
2. Jones MJ, Goodman SJ and Kobor MS (2015) DNA methylation and healthy human aging. Aging Cell 14(6):924-932.
3. Horvath S, Langfelder P and Kwak S, et al. (2016) Huntington's disease accelerates epigenetic aging of human brain and disrupts DNA methylation levels. Aging (Albany NY) 8(7):1485-1512.

4. Horvath S, Garagnani P and Bacalini MG, et al. (2015) Accelerated epigenetic aging in Down syndrome. Aging Cell. 14(3):491-495.
5. Horvath S and Levine AJ (2015) HIV-1 Infection Accelerates Age According to the Epigenetic Clock. The Journal of Infectious Diseases. 212(10):1563-1573.

Biography

Keith Booher has completed his dissertation research in the field of cancer cell metabolism at University of California, Irvine in 2011. After completing his PhD, he then accepted a Post-doc position developing methods and assays for the investigation of epigenetics at Zymo Research Corporation. Along with colleagues, he contributed to a high impact study evaluating methods for DNA methylation validation in 2016. He continues to conduct research in a commercial setting in his role as services projects manager at Zymo – with particular emphasis on epigenetics and microbiome analysis. His presentation will focus on the ability to quantify aging based on changing DNA methylation patterns at gene loci putatively involved in the aging process.

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