Forensic Individual Age Estimation with DNA: From Initial Approaches to Methylation Tests

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ABSTRACT: Individual age estimation is a key factor in forensic science analysis that can provide very useful information applicable to criminal, legal, and anthropological investigations. Forensic age inference was initially based on morphological inspection or radiography and only later began to adopt molecular approaches. However, a lack of accuracy or technical problems hampered the introduction of these DNA-based methodologies in casework analysis. A turning point occurred when the epigenetic signature of DNA methylation was observed to gradually change during an individual´s lifespan. In the last four years, the number of publications reporting DNA methylation age-correlated changes has gradually risen and the forensic community now has a range of age methylation tests applicable to forensic casework. Most forensic age predictor models have been developed based on blood DNA samples, but additional tissues are now also being explored. This review assesses the most widely adopted genes harboring methylation sites, detection technologies, statistical age-predictive analyses, and potential causes of variation in age estimates. Despite the need for further work to improve predictive accuracy and establishing a broader range of tissues for which tests can analyze the most appropriate methylation sites, several forensic age predictors have now been reported that provide consistency in their prediction accuracies (predictive error of ±4 years); this makes them compelling tools with the potential to contribute key information to help guide criminal investigations.

KEYWORDS: Age estimation, bisulfite conversion, DNA methylation, epigenetic age, epigenetic clock, forensic, statistical regression models.

INTRODUCTION

Forensic Context

Forensic age estimation can be used to gain information relevant to criminal, legal, or anthropological investigations [129]. First, the age of a person from analysis of their remains or from the biological traces they leave behind can help guide individual identification of a missing person or at the crime scene [2]. Multiple samples can be collected from the scene including hairs, bloodstains, semen, cigarette butts, and personal items such as toothbrushes. However, if DNA profiling does not lead to a match with any DNA database entries, no suspects can be identified. To overcome these barriers, forensic genetics is aiming to develop and validate new DNA intelligence tools. Rather than providing an individual-specific genetic profile, these new tests give information about characteristics that are shared by a much smaller group of potential suspects. Such characteristics include biogeographic ancestry [120] and externally visible characteristics (EVCs), alternatively termed phenotypic traits [78], that can create a more manageable pool of individuals sought by an investigation. Forensic DNA analysis could gain the same kind of advantage from the inference of individual age, as it is a clear feature of human appearance that is difficult to disguise. Second, the prediction of age-related physical traits, such as hair color or early-onset male pattern baldness, is improved by knowing the age of the DNA donor. Third, unidentified remains (of the missing, of victims of mass disasters, or of casualties in regions of conflict) are commonly encountered and are often challenging to identify if surviving relatives are not available [156]. In particular, mass disasters involve numerous samples that require detailed analysis in a short timeframe. Depending on the nature of the catastrophe, the remains will range in condition from relatively well preserved to highly degraded. Age estimation from DNA could therefore be used as a screening tool in order to accelerate the procedures or as supporting data in complex identifications. Fourth, the inference of age from DNA has considerable potential to add detail to the analysis of archeological remains [99]. Forensic anthropologists currently aim to identify a range of physical traits and the ancestry of ancient skeletal remains using established forensic DNA tests that could be extended to estimations of the age-at-death. Lastly; legal hearings could be supported by the inference of age from DNA samples taken from individuals whose age is in dispute, such as the likely age of an asylum seeker or the penalty applicable to young offenders [130]. This is a contentious issue, as the ascertainment of age in such matters requires a minimum level of accuracy and the way an estimate is obtained is invariably challenged in court on the basis of the technique's range of estimation values derived from its predictive error.

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Ana Freire-Aradas obtained her B.Sc. degree in pharmacy from the University of Santiago de Compostela (Spain) in 2006. In the same year she started her scientific research in the Forensic Genetics Unit, Institute of Forensic Sciences at the same university; obtaining her M.Sc. in molecular medicine in 2008 and her Ph.D. degree in 2013. After completing her Ph.D., Dr. Freire-Aradas continued her research in the same institution. Since 2015 she received a funding grant awarded by the Xunta de Galicia, Spain, as part of the Plan Galego de Investigación, Innovación e Crecemento 2011–2015; for supporting her postdoctoral research in both the Institute of Legal Medicine, University of Cologne (Germany), as host institution and the Institute of Forensic Sciences, University of Santiago de Compostela (Spain), as return institution. Research interests include SNP analysis for inference of biogeographic ancestry and externally visible characteristics; study of epigenetic markers such as DNA methylation with forensic applications, e.g., age estimation; evaluation of degraded DNA; and bioinformatic tools for assessment of DNA-based prediction models.

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