INPLASY PROTOCOL

To cite: Paparazzo et al. An ELOVL2 based epigenetic clock for forensic age prediction: a systematic review. Inplasy protocol 2022120006. doi: 10.37766/inplasy2022.12.0006

Received: 02 December 2022

Published: 02 December 2022

Corresponding author:
Alberto Montesanto

alberto.montesanto@unical.it

Author Affiliation:
University of Calabria

Support: **No fund.**

Review Stage at time of this submission: **Data analysis.**

Conflicts of interest:
None declared.

An ELOVL2 based epigenetic clock for forensic age prediction: a systematic review

Paparazzo, E[1]; Lagani, V[2]; Geracitano, S[3]; Citrigno, L[4]; Aceto, MA[5]; Malvaso, A[6]; Bruno, F[7]; Passarino, G[8]; Montesanto, A[9].

Review question / Objective: **To develop an easy, robust and improved blood-based age prediction model using ELOVL2 promoter methylation data.**
Eligibility criteria: **All studies with the aim of understanding the relationship between the ELOVL2 methylation levels and age written in English language, carried out in humans and providing a publicly available dataset will be included in the systematic review. Articles that did not include original research (e.g., review, opinion article or conference abstract) and for which methylation analysis will be carried out using a technology different from the pyrosequencing in tissues different form blood will be excluded from further analyses.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 02 December 2022 and was last updated on 02 December 2022 (registration number INPLASY2022120006).

INTRODUCTION

Review question / Objective: **To develop an easy, robust and improved blood-based age prediction model using ELOVL2 promoter methylation data.**

Rationale: **The prediction of chronological age from methylation-based biomarkers represents one of the most promising applications in the field of forensic sciences. The age prediction models so far developed were not easily applicable in forensic caseworks. Among the several attempts to pursuit this objective, the formulation of single-locus models might represent a good strategy.**

Condition being studied: **Age prediction using methylation data.**

METHODS

Search strategy: A systematic search was carried out in SCOPUS and PUBMED databases. A manual search in the bibliographies of selected articles was also conducted. The following Boolean search strings were used considering free text and Medical Subject Heading.
PubMed/MEDLINE: ((((ELOVL fatty acid elongase 2[All Fields]) OR ELOVL2[All Fields])) AND (((Age[Title/Abstract]) OR aging[Title/Abstract]) OR ageing[Title/Abstract]) AND (pyrosequencing[All Fields])
Scopus: ((ALL (ELOVL AND fatty AND acid AND elongase AND 2) OR ALL (ELOVL2))) AND ((TITLE-ABS-KEY (age) OR TITLE-ABS-KEY (aging) OR TITLE-ABS-KEY (ageing))) AND (ALL (pyrosequencing)).

Participant or population: Healthy human subjects.

Intervention: Not applicable.

Comparator: Not applicable.

Study designs to be included: There will be no restrictions on the types of study design eligible for inclusion in this review. Any publications that are not in written English will be excluded from the review.

Eligibility criteria: All studies with the aim of understanding the relationship between the ELOVL2 methylation levels and age written in English language, carried out in humans and providing a publicly available dataset will be included in the systematic review. Articles that did not include original research (e.g., review, opinion article or conference abstract) and for which methylation analysis will be carried out using a technology different from the pyrosequencing in tissues different form blood will be excluded from further analyses.

Information sources: The following databases will be used: SCOPUS, PUBMED. Also, key journals and reference lists will be searched for additional references. There will be no publication date restriction to avoid excluding papers identified in non-indexed papers. The search date for each database will be reported.

Main outcome(s): Correlation of ELOVL2 methylation variability and chronological age. Several Machine Learning approaches for the development of ELOVL2 single-locus age prediction models will be tested.

Additional outcome(s): Not applicable.

Quality assessment / Risk of bias analysis: We will use blinding methods among authors using Covidence. Moreover, disagreements between reviewers will be resolved thanks to a third reviewer/help of expert opinion. The final dataset that will be obtained and analysed will be randomly split in half, creating a training and a validation set. The split will be performed in such a way to obtain the same age distribution between training and test set. The training set will be then used for creating a number of predictive models able to provide age estimates for single individuals, while the validation set will be used for unbiasedly assess the predictive capabilities of each model.

Strategy of data synthesis: All eligible datasets will be appropriately merged. The resulting comprehensive dataset will be randomly split in half, creating a training and a validation set. The split will be performed in such a way to obtain the same age distribution between training and test set. The training set will be then used for creating a number of predictive models able to provide age estimates for single individuals, while the validation set will be used for unbiasedly assess the predictive capabilities of each model. The predictive capabilities of each age prediction model will be evaluated through the mean absolute error (MAE) metric.

Subgroup analysis: There is no plan for subgroup analysis.

Sensitivity analysis: Sensitivity analysis will performed using a leave-dataset-out approach.

Language restriction: Only publications that are written in English will be included in the review.

Country(ies) involved: Italy.

Keywords: ELOVL2, age prediction, methylation.

Dissemination plans: The review findings will be published in peer-reviewed journals.

Contributions of each author:

Author 1 - Ersilia Paparazzoa - E.P. critically reviewed this protocol and also contributed to the data extraction. She will also contribute to the statistical analysis and preparation of the manuscript of this review.
Email: ersilia.paparazzo@unical.it
Author 2 - Vincenzo Lagani - V.L. critically reviewed this protocol and will also contribute to the statistical analyses and preparation of the manuscript of this review.
Email: vincenzo.lagani@iliauni.edu.ge
Author 3 - Silvana Geracitano - S.G. critically reviewed this protocol and contributed to the data extraction; She will also contribute to manuscript preparation of this review.
Email: silvana.geracitano@unical.it
Author 4 - Luigi Citrigno - L.C. critically reviewed this protocol and and will contribute to the manuscript preparation of this review.
Email: luigi.citrigno@irib.cnr.it
Author 5 - Mirella Aurora Aceto - M.A.A. critically reviewed this protocol and also contributed to the data extraction. She will also contribute to the statistical analysis and preparation of the manuscript of this review.
Email: auroraaceto@gmail.com
Author 6 - Antoinio Malvaso - A.M. critically reviewed this protocol and will lead the selection and data extraction processes and the risk of bias assessment.
Email: malvaso.antonio@libero.it
Author 7 - Francesco Bruno - F.B critically reviewed this protocol and will contribute to the manuscript preparation of this review.
Email: francescobrunofb@gmail.com
Author 8 - Giuseppe Passarino - G.P. critically reviewed this protocol and will also contribute to the preparation and finalisation of the manuscript of this review.
Email: giuseppe.passarino@unical.it
Author 9 - Alberto Montesanto - A.Mo. developed and prepared the review protocol and will also contribute to the selection and data extraction processes. A.Mo. will also contribute to the preparation the manuscript of this review.
Email: alberto.montesanto@unical.it