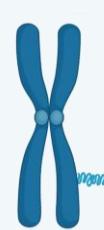
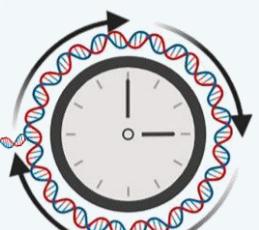


# Exploring a Deep Learning Epigenetic Clock Based on an Interpretable Convolutional Neural Network to Unravel the Tick-Tock of Cellular Aging

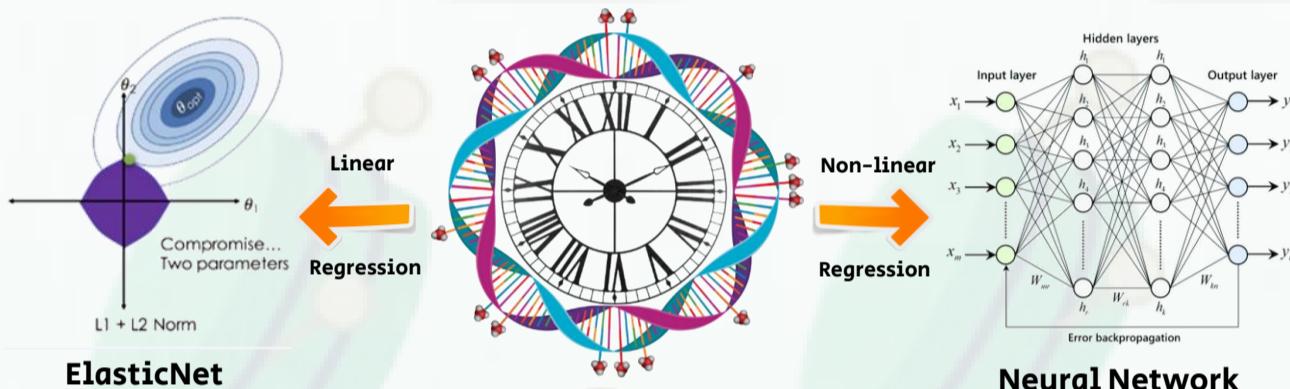
Enrique Roig-Tormo<sup>a</sup>, Vladimiro Diaz-Villanueva<sup>b</sup> and Carlos Peña-Garay<sup>a,b</sup>

a. Laboratorio Subterráneo de Canfranc (LSC), Canfranc-Estación, Huesca, Spain

b. Institute for Integrative Systems Biology (I<sup>2</sup>SysBio), Universitat de València-CSIC, Valencia, Spain

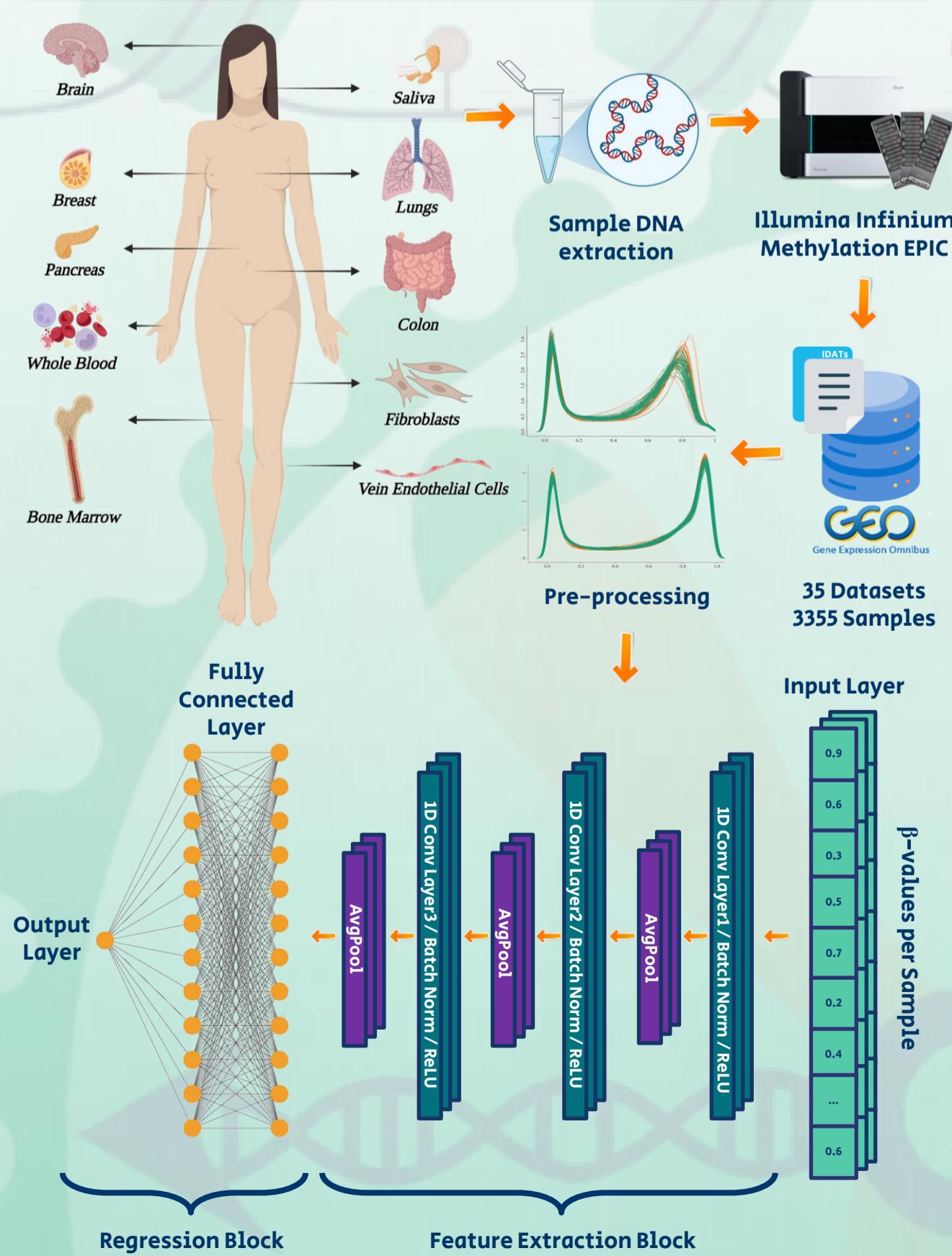
## INTRODUCTION

DNA methylation patterns have emerged as valuable epigenetic biomarkers, modeling aging-related molecular changes through so-called epigenetic clocks. These clocks have traditionally relied on linear regression models, for both feature selection and age prediction [1, 2, 3]. However, linear models have limited ability to capture nonlinear interactions and spatial dependencies between CpG sites. For this reason, recent approaches have turned to deep learning methods, which are better suited to modeling complex relationships [4, 5, 6].



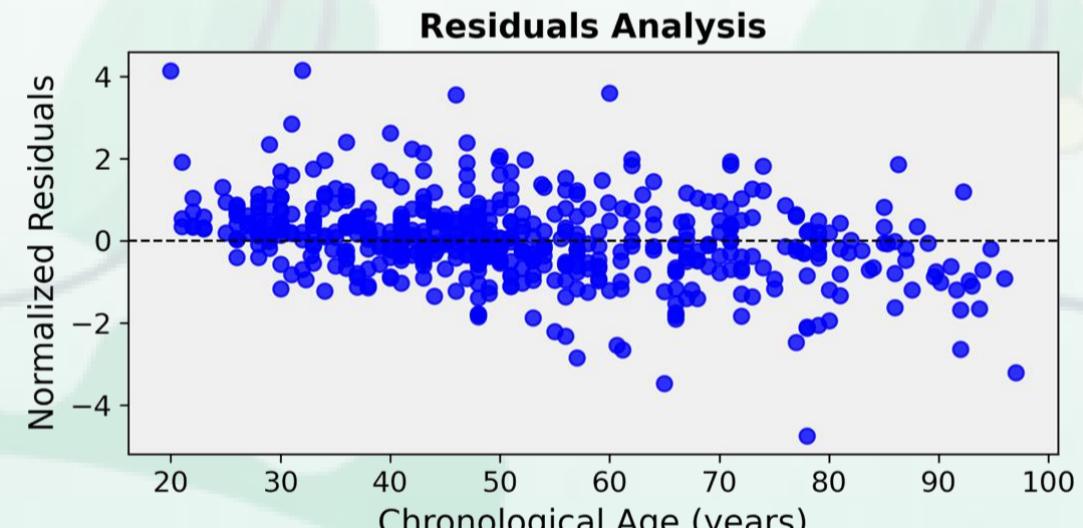
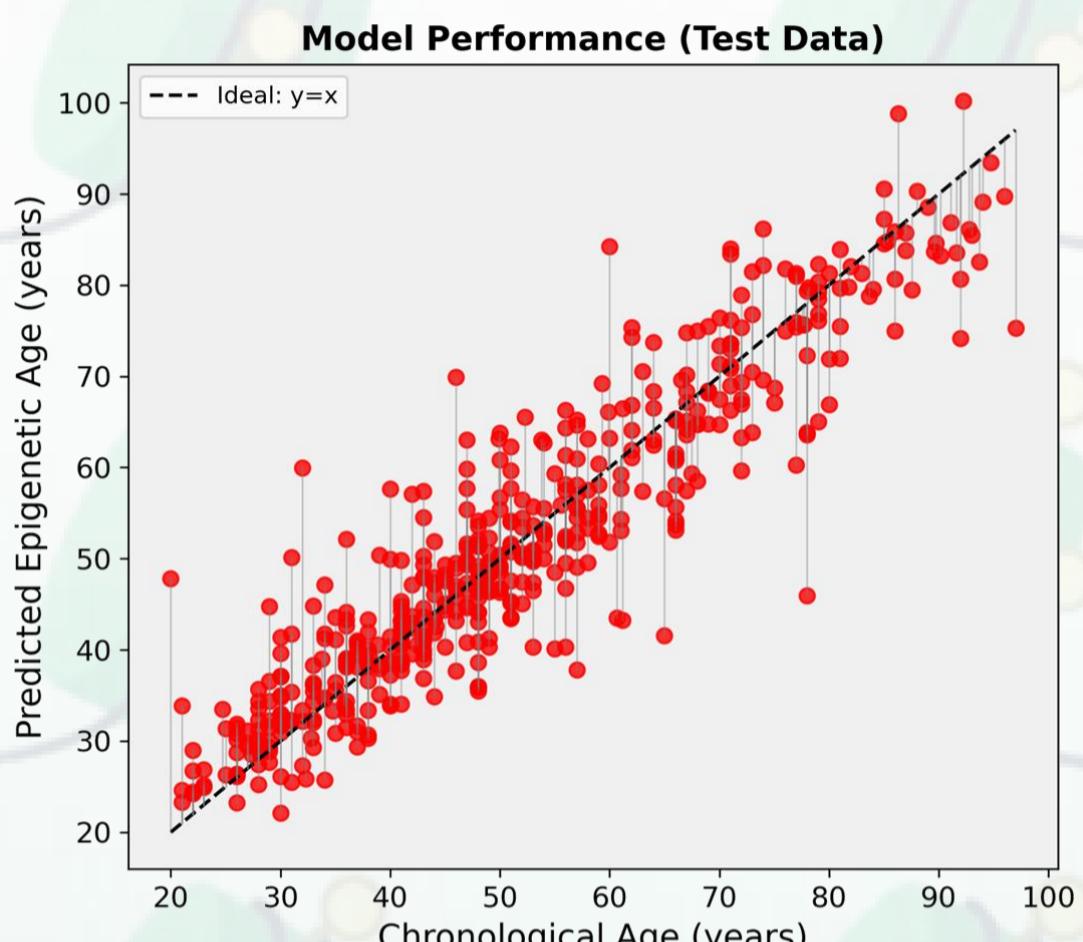
This study aims to develop a multi-tissue epigenetic clock using an interpretable convolutional neural network trained on methylation maps that spatially organize CpG sites by their genomic positions. The model seeks to improve age prediction accuracy and to identify genomic regions associated with aging-related epigenetic changes.

## METHODOLOGY



## RESULTS

The developed epigenetic clock shows high performance in an independent test set, with an  $R^2 = 0.853$  and an RMSE of 6.74 years. These results indicate good generalization capability of the model and support its robustness in reliably capturing the epigenetic signal associated with aging.



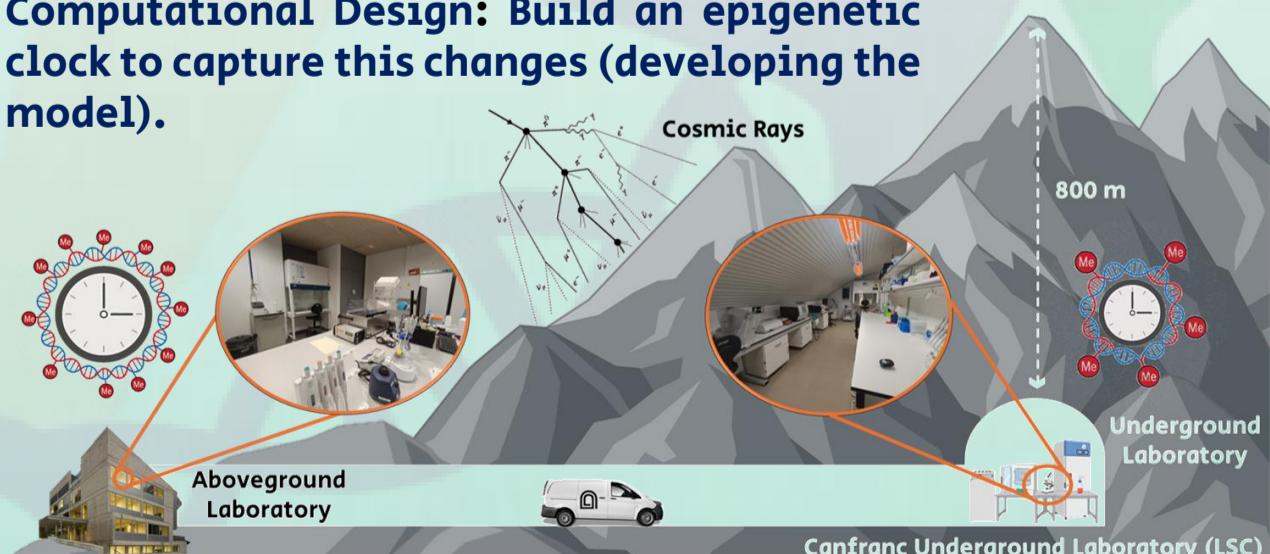
## NEAR FUTURE

Observe the impact on epigenetic changes associated with aging in space travels. To this end, space conditions will be simulated in the Canfranc Underground Laboratory:

**Microgravity**   **Absence of secondary cosmic rays ( $\mu$ )**   **Presence of primary cosmic rays ( $p^+$ )**

**Experimental Design:** Proton irradiation of fibroblast cells which have been exposed to microgravity underground.

**Computational Design:** Build an epigenetic clock to capture these changes (developing the model).



## REFERENCES

1. Bocklandt, S., et al. (2011). PloS one, 6(6), e14821.
2. Horvath S. (2013). Genome Biology, 14.
3. Hannum G, et al. (2013). Mol Cell. 49(2):359-367.
4. Prosz, A., et al. (2024). Sci Rep, 14, 1306.
5. de Lima Camillo, L.P., et al. (2022). npj Aging, 8, 4.
6. Sharma, A., et al. (2021). Brief. Bioinform., 22(6).