

AI- based retinol signature: identification of new best-in-class anti-aging ingredients

**IFSCC2025
-1724**

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INTRODUCTION

Skin aging is a complex multifactorial process influenced by both intrinsic factors and extrinsic stressors. Twelve interrelated biological hallmarks contribute to its visible signs [1]. Retinol is the gold standard in anti-aging ingredients, [2,3] and the development of retinol-like active ingredients has emerged with a growing interest. Thus, it is particularly interesting to establish a model able to assess the anti-aging potential of a compound.

MATERIALS & METHODS

In this study, we developed an AI-driven method to measure retinol dedicated effect in aging by analyzing 50 genes among twelve hallmarks of skin aging. To do this, fibroblasts from four donors (62, 67, 23 and 28) were treated with Retinol and gene expression were assessed by RT-qPCR.

The twelve hallmarks of skin aging					
Autophagy reduction	Chronic inflammation	Senescence	Nutrient sensing	Stem cells exhaustion	Mitochondria dysfunction
Loss of proteostasis	Genomic instability	Telomere attrition	Intercellular communication	Epigenetic alterations	Dysbiosis

Then, a logistic regression was trained to discriminate between old samples on one side ($y_i = -1$), and old samples treated with Retinol and young ones on the other side ($y_i = 1$), based on the qPCR gene expression profiles (X_i). The model was fit by minimizing the function :

$$\min_{\beta} \sum_i \mathcal{L}(X_i, y_i, |\beta|) + \lambda \|\beta\|_1, \text{ where } \mathcal{L} \text{ is the logistic loss.}$$

Using the L1 loss led to sparse features, we identified 8 genes whose expression had the most potential to predict young profile of cells treated with retinol. Those genes defined the retinol-like signature.

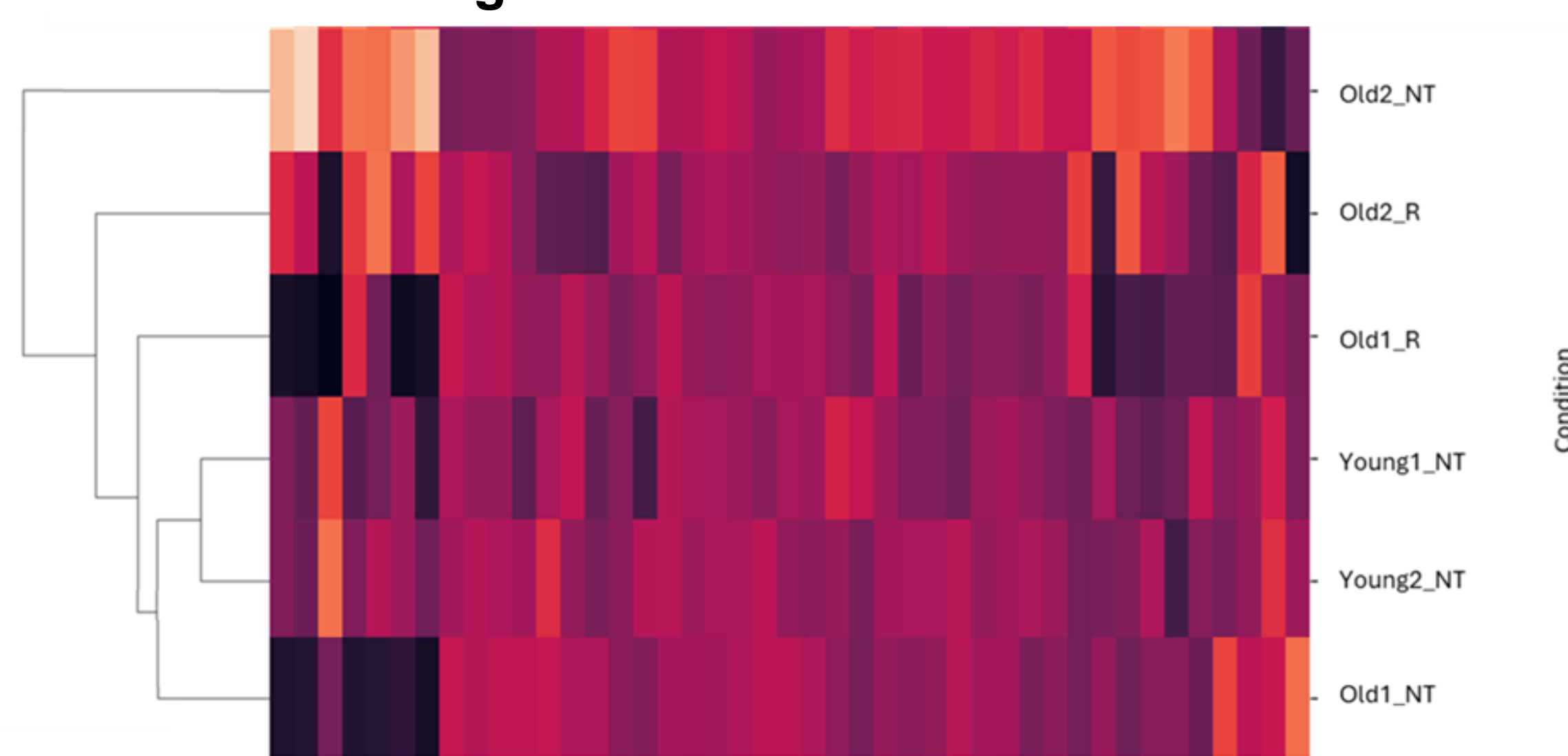
We trained a support vector model on the same data, keeping only the 8 signature genes' expression profiles. We extracted from the model a score that predicted the anti-aging potential of the ingredients:

$$S(x) = \sum_i y_i w_i K(x_i, x) + w_0, \text{ where } w_i \text{ are the trained weights, and } K \text{ is the RBF kernel: } K(x, x') = e^{-\gamma \|x - x'\|^2}$$

Finally, we used this reliable signature to test the efficacy of promising anti-aging ingredients such as Astragaloside 4 (AS4) and GLYULT1, a novel metabiotic derived through multi-fermentation

RESULTS

1) Retinol effect on 50 genes from the 12 hallmarks



Visualization of gene expression profiles for 50 genes. Values are shown in CT units : higher values means lower expression, which are represented by lighter colors. Hierarchical clustering (on the left) was then performed using the distance between gene expression profiles. R. Retinol, NT. Non-treated.

CONCLUSION

The study introduced a new AI-driven, retinol-based anti-aging signature that can discriminate between young and aged cells. This signature of 8 genes was enriched with a quantifiable score. This leads to a holistic approach that enhances the exploration of retinol alternatives and supports the development of innovative anti-aging strategies.

References

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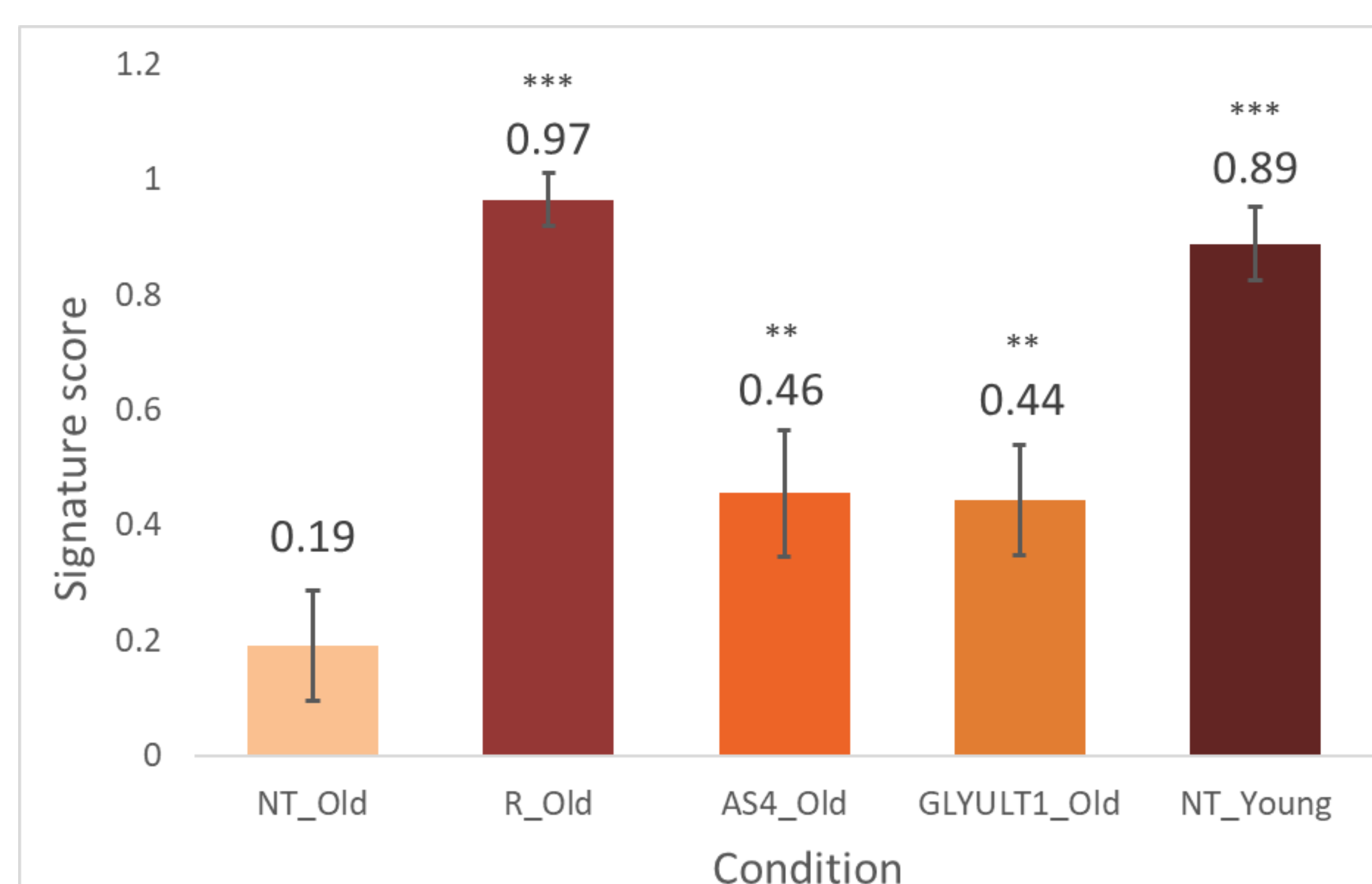
Young donors clustered together in the same branch, while aged donors were in opposite branches. This result is in accordance to the fact that aging is known to increase transcriptional noise [4]. Retinol treatment clustered the two older donors and the younger ones together. This suggested that retinol treatment may reduce transcriptional noise due to age.

2) Retinol signature



Visualization of gene expression profiles for 8 signature genes. Values are shown in CT units : higher values means lower expression, which are represented by lighter colors. Hierarchical clustering (on the left) was then performed using the distance between gene expression profiles. R. Retinol, NT. Non-treated.

Young donors and retinol treated aged donors are clustered in two branches next to each other. The aged donors are far apart.



Retinol signature score. The gene expression profile of each sample was analyzed using the age signature model. Resulting scores were averaged for each condition. The error bars represent the standard error of the mean. Student t-test were performed against the untreated old condition (**p-value < 0.005, ***p-value < 0.001). R. Retinol, AS4. Astragaloside IV, NT. Non-treated.

An average of the "youthful" score of the two donors showed that :

- retinol-treated donors scored similarly to young donors, reaffirming its strong anti-aging effect by closely aligning with a youthful biological profile.
- AS4 and GLYULT1 displayed better scores than aged NT donors. While AS4 and GLYULT1 demonstrated comparable efficacy, their effects were less pronounced than retinol. Nonetheless, these results highlighted their significant potential as anti-aging ingredients, with GLYULT1 standing out as a promising candidate for further exploration.