Atavistic Genetic Expression Dissociation (AGED) during aging: meta-phylostratigraphic evidence of cellular- and tissue-levels phylogenetic dissociation

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Abstract:

Aging is commonly attributed to accumulated damage, or evolved antagonistic genetic trade-offs, which lead to an accumulation of genetic damage, noise, or DNA methylation causing the misexpression of key genes necessary for longevity. We propose an atavistic dysregulation of gene expression at cellular and tissue-levels during aging, which frames aging as a gradual regression toward ancestral cellular states. Similar to the atavistic model of cancer, in which cells revert to unicellular-like behavior, aging may result from a progressive breakdown of coordinated morphogenetic control, leading organs and tissues to revert towards less integrated, ancient unicellular states. This view suggests that aging may involve a progressive reversal of the well-known ontogenetic tracing of prior phylogenetic embryonic characteristics. Moreover, as in cancer, aging could involve a loss of large-scale coordination, with different tissues reverting to ancient gene expression to different degrees. We tested this hypothesis using a meta-phylostratigraphic analysis to ask: do older human tissues express more ancient genes, and does the variance of transcriptional phylogenetic age across tissues increase with organismal age? We found: (1) An atavistic over-representation of differential expression in the most ancient genes for two multi-tissue aging databases covering skin, ovarian, immune, senescent and mesenchymal-senescent cells; (2) No atavistic over-representation of the differential genet expression during aging of brain cells and mesenchymal stem cells; and (3) overall age-dependent increase of heterogeneity in the direction of the phylogenetic position of tissues' transcriptional profiles. Our analyses suggest that aging involves uncoordinated and tissue-specific phylogenetic changes in gene expression. Understanding aging as a structured, heterogenous atavistic process opens new avenues for rejuvenation, focusing on restoring multicellular coherence with respect to evolutionarily-youthful gene expression.

1. Introduction

1.1 Aging theories

Most complex organisms experience a sequential life course consisting of embryonic development stages, growth to maturity, and then functional decline and ultimately death. Aging leads to progressive deterioration of cellular structures and biological functions in living systems [1-4]. The aging process is influenced by diverse elements including genetic inheritance, environmental conditions, and behavioral choices[5]. The resistance of biological systems to noise and damage decreases with age[6-8], leading to health issues including cardiovascular complications, cancer, neurodegenerative disorders, metabolic disruptions such as type II diabetes, and compromised immune responses to pathogens, which strongly impact quality of life [2, 5, 9, 10].

The scientific community has been focused on two main theoretical frameworks to understand the aging process: damage-based [2, 9] and programmatic [1-3, 11-15] theories. Damage-based theories hold that aging results from the inevitable accumulation of molecular damage over time. Essential cellular components including genetic stability, telomere length, mitochondrial activity, and protein homeostasis experience severe degradation. In contrast, programmatic theories propose that aging is the evolutionary result of a genetically-encoded biological trajectory. This perspective suggests that the aging process is encoded in our genome, because it provides reproductive advantage at the lineage level, rather than merely representing stochastic damage accumulation over time [16-18].

1.2 Longevity as the result of anatomical homeostasis

A novel direction with respect to aging is suggested by a focus on morphogenesis and morphostasis (cellular self-assembly into complex anatomical forms, and continued maintenance of the correct structure) as active navigation of anatomical morphospace [19-24]. This framework sees embryogenesis, regeneration, and cancer suppression as a continuous dynamic set of decisions made by the cellular collective to reach and maintain organ-level target morphologies [19, 22, 25]. Numerous tools from behavioral neuroscience and cybernetics have been deployed in morphogenetic systems to probe the mechanisms which coordinate cells toward common anatomical endpoints [21, 22, 26, 27]. The ability to reach and maintain species-specific large-scale anatomical states reliably, despite noise and perturbations, is a kind of homeostatic dynamic that has been modeled as a collective intelligence [28], with many applications in biomedicine across birth defects and regeneration [29, 30]. Moreover, this approach has provided novel ways to address cancer as a loss of coordination of cells toward tissue-level homeostatic goals[31-33]. From this perspective, one can ask what kind of information-processing disorders could contribute to aging as a long-term loss of the ability to organize cells and subcellular materials toward maintenance of a healthy complex form.

We recently proposed that aging is the result of the loss of morphostatic information [34, 35]. In this framework, aging is an emergent failure mode of information-processing

collectives that lose morphogenetic guidance after construction of the adult body structure has been completed [34, 35]. What kind of directional changes might be observed in cells and tissues after the primary anatomical goals have been met, in addition to loss of precision and random alterations? Moreover, when not bound to a single (body-wide) anatomical setpoint as occurs during embryogenesis, would different cells in the body eventually adopt distinct setpoints, thus resulting in loss of coherent function as observed in aging?

The setpoints for anatomical homeostasis in evolved creatures are shaped by evolution [36-42]; specifically, they are determined by phylogenetic position and the body-plan it specifies. Could the kind of dissociation of self-model from reality that is observed in certain psychological disease states [43, 44] have a somatic counterpart, in which the actual phylogenetic age of cells (*Homo sapiens*) becomes dissociated from the *effective* physiological phylogenetic age due to the expression of more ancient genes? We sought to ask: what is the relationship between an organism's age and the phylogenetic information its tissues attempt to implement? Using transcriptional profiling datasets, and phylostratigraphy [45-47] to analyze the evolutionary age of genes being expressed in specific tissues, we tested two hypotheses. First, that aging involves a roll-back of transcriptional profiles to include more ancient genes (in effect, a reversal of the well-known "ontogeny recapitulates phylogeny" dynamic with respect to embryonic patterns). Second, that this would include a significant loss of *coordination* across the body, in which different tissues ended up phenocopying the transcriptional states of different positions across phylogenetic history, similarly to what occurs in cancer [31, 48-50].

1.3 The atavistic disregulation hypothesis of aging

We tested this hypothesis using a meta-phylostratigraphic analysis. We applied a phylostratigraphic analysis using RNA-seq and scRNA-seq data from 8 different studies two meta-analyses including different tissues RNA-seq during aging [51, 52], scRNAseq data from skin cells[53], an aging meta-analysis of the scRNA-seq of senescent cells [54], and brain (cortex, hippocampus and cerebellum cells) [55], immune[56], ovarian [57] and stem cells RNA-seq [58] (see Table 1). We found the following: (1) An atavistic over-representation of differential expression in the most ancient genes for two multi-tissues aging databases covering skin, ovarian, immune, senescent and mesenchymal-senescent cells; (2) No atavistic over-representation of the differential genet expression during aging of brain cells and mesenchymal stem cells; and (3) overall age-dependent increase of heterogeneity in the direction of the phylogenetic position of tissues' transcriptional profiles. Thus, we propose that while cancer is a loss of cellular organization in space, aging involves a loss of cellular organization in (evolutionary) time.

2 Material and methods

We applied a meta-phylostratigraphic analysis using RNA-seq and scRA-seq data from 8 different studies two meta-analyses including different tissues RNA-seq during aging [51, 52], scRNAseq data from skin cells[53], an aging meta-analysis of the scRNA-seq of senescent cells[54], and brain (cortex, hippocampus and cerebellum cells)[55], immune[56], ovarian [57] and stem cells RNA-seq [58] (see Table 1).

Cell types	All tissues, meta-analysis		Skin cells		Senescent cells	Brain cells			Immune cells	Ovarian cells	Stem cells		
Data	Age-related genes		scRNA-seq, 40-70 years old	scRNA-seq, >70 years old	Meta-analysis	Brain cortex	Hippocampus	Cerebellum	CD8T	Ovary	MSC	MSC-senescent	HPC
References	[51]	[52]	[53]		[54]	[55]			[56]	[57]	[58]		

Table 1: Table of all datasets used in this study for the phylostratigraphic meta-analysis of aging genetic expression. 8 datasets were used, several of them are meta-analyses totalizing more than 100 datasets.

To analyze the differentially expressed genes (DEGs) in the aging cells under various conditions through phylostratigraphic analysis, we used the evolutionary ages of 19,660 human protein-coding genes as determined by Litman et al.[59]. These genes were categorized into 19 major phylostrata, as outlined by Domazet-Loso and Tautz[46]. The phylostrata are a hierarchical range of evolutionary origins for: All living organisms (including Eubacteria, Bacteria and their descendants, e.g. unicellulars), Eukaryota, Opisthokonta, Holozoa, Metazoa, Eumetazoa, Bilateria, Deuterostomia, Chordata, Olfactores, Craniata, Euteleostomi, Tetrapoda, Amniota, Mammalia, Boreoeutheria, Eutheria, Euarchontoglires, and Primates.

We quantified the number of genes expressed under the various experimental conditions to assess the atavistic patterns we may find during aging in terms of genetic expression. We then applied an overrepresentation test for each group of genes in each phylostrata compared to the ensemble of ages of all human protein-coding genes. The overrepresentation test (also known as enrichment analysis) is a widely used statistical to determine whether a specific set of elements (e.g., genes, proteins, or other features) is significantly overrepresented in a given category compared to a background distribution. Overrepresentation tests are extensively used in various scientific fields, particularly in Gene Ontology (GO) Enrichment Analysis where we identify functional categories overrepresented in a set of differentially expressed genes[60], Pathway Enrichment Analysis where we assess whether biological pathways, such as KEGG pathways, are significantly enriched in a dataset [61] and Disease Association Studies where we link genetic variants to diseases by testing for enrichment in disease-associated categories[62]. This approach is crucial for understanding biological processes, molecular pathways, and functional annotations associated with high-throughput data.

More specifically, in our case, given a "gene universe**"** (here the list of all human protein-coding genes) containing N total genes, this test evaluates whether a specific phylostratigraphic category is statistically overrepresented within a smaller subset of n genes selected from this gene universe in a specific condition. With M genes belonging to a specific phylostratigraphic category in the gene universe, the test calculates the probability of

observing k genes from this functional category within the selected subset of n genes randomly, using the hypergeometric distribution:

$$P(X = k) = \frac{\binom{M}{k}\binom{N-M}{n-k}}{\binom{N}{n}}$$

A p-value is then calculated to determine the significance of the overrepresentation of the observed enrichment. Here we use a p-value inferior to 0.05 to determine the significance.

3 Results

3.1 Atavistic over-representation in the most ancient genes for multi-tissues aging signatures (GenAge and AgeMeta)skin, ovarian, immune, senescent and mesenchymal-senescent cells.

We applied the phylostratigraphic analysis on two multi-tissue aging datasets. The first signature was extracted from GenAge [51] and has been extracted from 127 publicly available microarray and RNA-Seq datasets from mice, rats and humans, identifying a transcriptomic signature of aging across species and tissues (brain, heart and muscle). The second one is likewise a meta-analysis of 51 humans scRNA-seq datasets of different tissues (vastus lateralis, cerebellum, frontal cortex, muscle, brain, adipose tissue, adrenal gland, blood, blood vessel, brain (without cerebellum), esophagus, heart, lung, nerve, pituitary, salivary gland, prostate, testis, and thyroid). We observed in both aging signature an over-representation of the most ancient genes in the 'All living organisms' strata (see Figure 1). The GenAge aging signature show more over-representations, notably in Ospithokonta, Holozoa, Eumetazoa, Bilateria and Euteleostomi stratas while the human AgeMeta signature shows only one over-representation in the unicellular genes. The number of upregulated and downregulated genes in the most ancient genes in the GenAge aging signature is almost equal, suggesting more a reshuffling in the genetic expression during aging in the most ancient genes. The AgeMeta aging signature is dominated by downregulated genes in the 'All living organisms' strata.

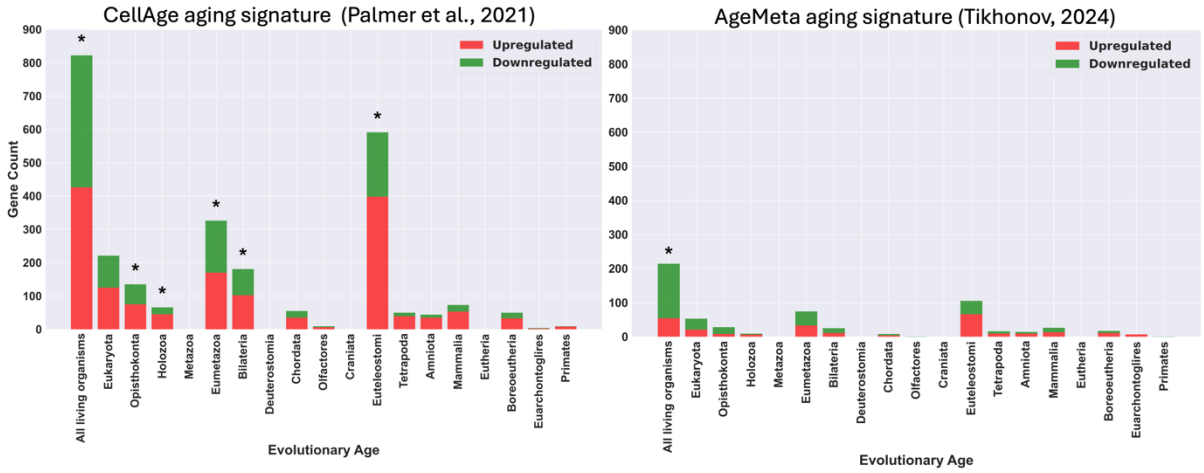

Figure 1: Atavistic over-representation observed in the GenAge and AgeMeta aging signatures. The figures illustrate gene expression changes in different cell types (skin, immune, and ovarian cells) across evolutionary age categories. The bar charts separate genes into upregulated (red) and downregulated (green) categories, providing insight into how aging influences gene regulation across different phylogenetic layers. The star above a bar chart means that the over-representation test is significant (p-value<0.05).

We conclude that we have an atavistic over-representation of differentially expressed genes in both aging signature with a heterogeneity in the direction of the genetic changes.

3.1.2 Atavistic over-representation during aging in skin, ovarian, immune, senescent and mesenchymal-senescent cells.

We applied the phylostratographic analysis to skin, ovarian and immune scRNA-seq. For skin cells, in both age groups, gene expression changes are most significant in early evolutionary categories (e.g., "All living organisms" and "Eukaryota"). Genes from more recent evolutionary branches (e.g., "Primates," "Euarchontoglires") showed fewer expression changes. A shift is observed in gene counts across aging, with a decrease in downregulated genes in the oldest group. In the 40-70 years age group, genes belonging to "All living organisms" show the highest number of expression changes, with a stronger contribution from downregulated genes. In individuals older than 70, the "Euteleostomi" category showed a significant increase in gene expression changes, particularly upregulation. A notable decrease in gene expression changes is seen in "All living organisms" in the >70 group compared to the 40-70 group of fibroblasts (see Figure 2).

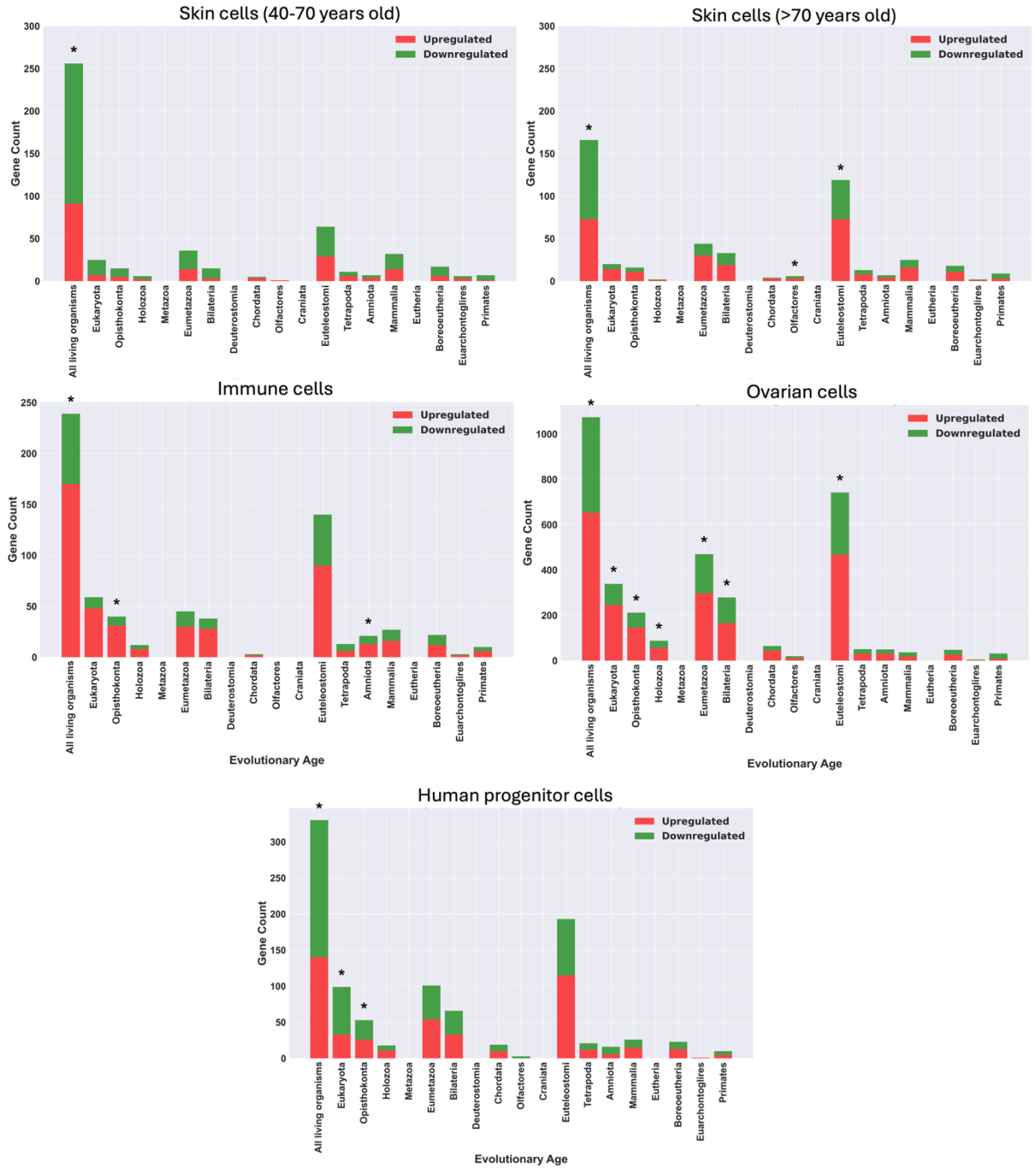

Figure 2: Atavistic over-representation observed in the skin, immune and ovarian cells. The figures illustrate gene expression changes in different cell types (skin, immune, and ovarian cells) across evolutionary age categories. The bar charts separate genes into upregulated (red) and downregulated (green) categories, providing insight into how aging influences gene regulation across different phylogenetic layers. The star above a bar chart means that the over-representation test is significant (p-value < .05).

As in skin cells, the highest number of differentially expressed genes in immune cells was found in "All living organisms" and "Eukaryota." Compared to skin cells, immune cells exhibited fewer gene expression changes overall. "Euteleostomi" showed a high number of differentially expressed genes, similar to the oldest group in skin cells. Upregulated genes were more important in the most ancient genes (see Figure 2).

Ovarian cells showed the highest total number of differentially expressed genes among all cell types. The most significant gene expression changes occurred in ancient evolutionary categories. A strong signal of gene regulation is observed in "Cranial" and "Euteleostomi." "All living organisms" and "Eukaryota" categories showed over 1000 differentially expressed genes (see Figure 2). Ovarian cells show a higher level of gene expression shifts compared to immune and skin cells, possibly reflecting the pronounced effects of aging in reproductive tissues.

Human progenitor cells showed a significant atavistic over-representation in the “All living organisms”, “Eukaryota” and “Ospithokonta” evolutionary ages (see Figure 2). We observed mostly down-regulation in the genetic expression of these over-representations of evolutionary ages.

In the senescent signature, gene expression changes are most pronounced in ancient evolutionary categories, with "All living organisms" showing the highest level of differentially expressed genes, dominated by downregulation. The categories "Eukaryota" and "Eumetazoa" also exhibit significant regulation, with a mix of upregulated and downregulated genes. A smaller but notable increase in gene expression changes is seen in "Cranial" and "Euteleostomi," suggesting that vertebrate-specific pathways contribute to cellular senescence (see Figure 3).

Mesenchymal senescent cells followed a similar trend, with "All living organisms" and "Eukaryota" showing substantial gene expression changes, though the magnitude is slightly higher than in the general senescent signature. Compared to the general senescence profile, mesenchymal senescent cells exhibited an increased upregulation in "Cranial" and "Euteleostomi," reinforcing the idea that vertebrate-specific genes play a role in mesenchymal aging and senescence-related processes (see Figure 3).

Overall, we conclude that there is an atavistic overrepresentation in the differential genetic expression during aging in skin, immune, ovarian and human progenitor cells associated to a heterogeneity in the direction of the changes, sometimes the atavistic change is more about downregulation (skin cells), sometimes the opposite with more upregulation in the most ancient genes (immune and ovarian cells).

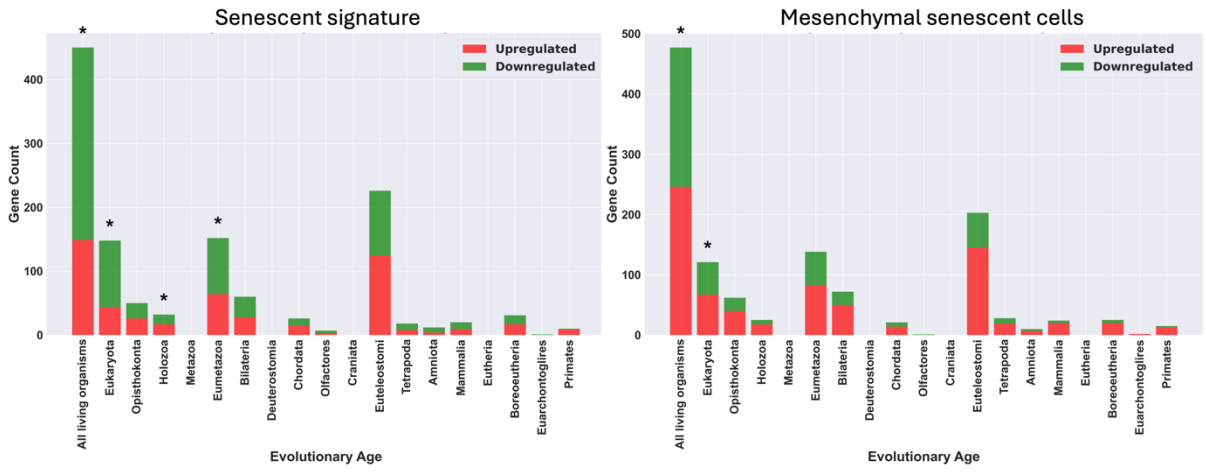

Figure 3: Atavistic over-representation found in the senescent genetic signature and mesenchymal-senescent cells. The figures illustrate gene expression changes in different cell types (skin, immune, and ovarian cells) across evolutionary age categories. The bar charts separate genes into upregulated (red) and downregulated (green) categories, providing insight into how aging influences gene regulation across different phylogenetic layers. The star above a bar chart means that the over-representation test is significant (p-value < .05).

3.2 No atavistic genetic over-representation during aging in brain cells and mesenchymal stem cells

Cerebellum and hippocampus and cortex cells exhibited similar patterns, with the highest number of differentially expressed genes occurring in the “Euteleostomi” strata. This category showed mainly upregulation for the hippocampus, and more downregulation for the two more types of brain cells, suggesting increased reliance on vertebrate-specific pathways during aging for the brain. There is no genetic atavistic over-representation, the DEGs are indeed not significantly over-represented in the “All living organisms” strata (Figure 4).

The mesenchymal cells, in contrast, showed a lower total number of differentially expressed genes compared to brain cells but maintain the same evolutionary hierarchy in gene regulation. We had a significant over-representation of DEGs in "Euteleostomi" but no significant atavistic over-representation in the “All living organisms” strata (Figure 4).

We can conclude there is no atavistic over-representation of the genetic changes in the most ancient genes for brain and mesenchymal stem cells suggesting a differential aging or resistance to aging for the brain tissue and stem cells, as suggested by [63, 64].

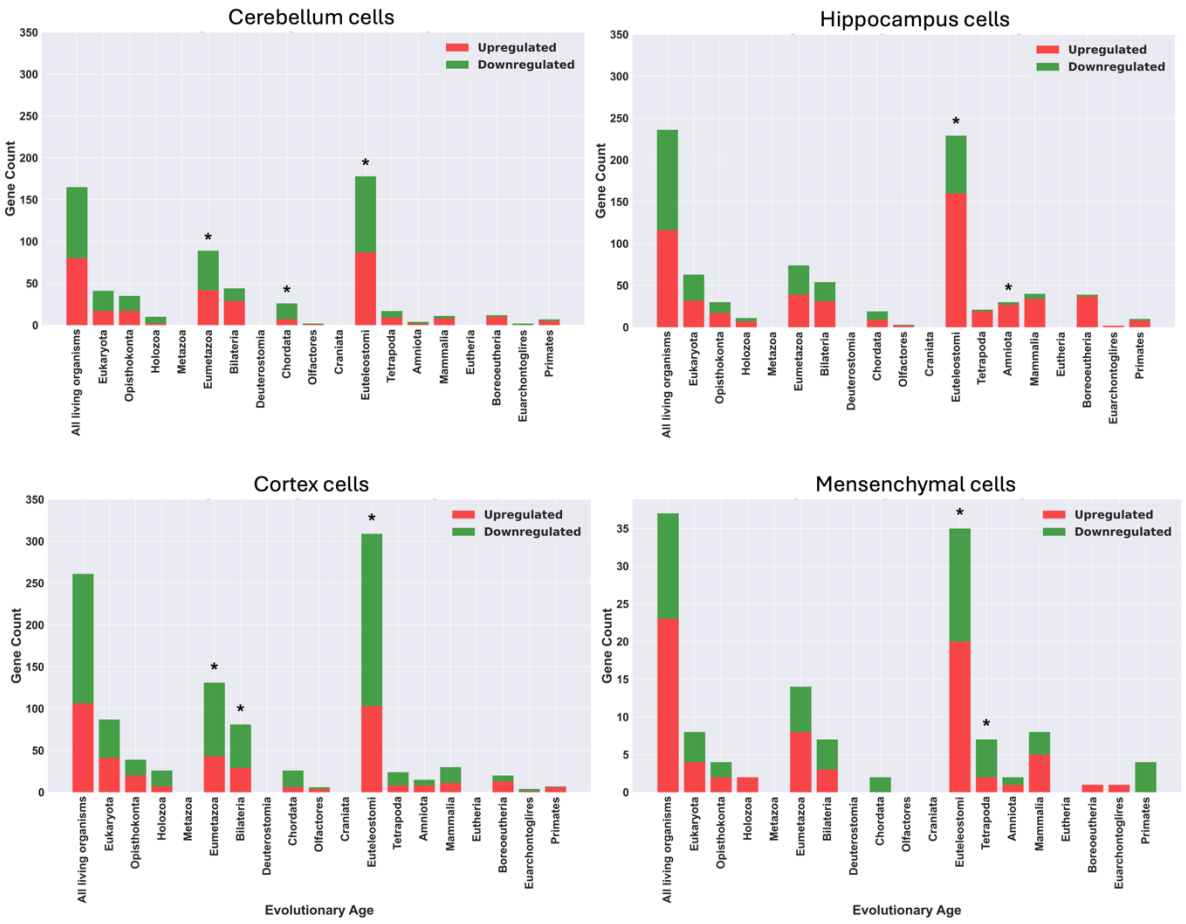

Figure 4: No atavistic genetic over-representation is found during aging in brain cells and mesenchymal stem cells . The figures illustrate gene expression changes in different cell types (skin, immune, and ovarian cells) across evolutionary age categories. The bar charts separate genes into upregulated (red) and downregulated (green) categories, providing insight into how aging influences gene regulation across different phylogenetic layers. The star above a bar chart means that the over-representation test is significant (p-value < .05).

3.3 Atavistic dysregulation of the most ancient genes during aging

Overall, we found an age-dependent increase of heterogeneity in the direction of the phylogenetic position of tissues' transcriptional profiles. The number of upregulated and downregulated genes in the most ancient genes in the GenAge aging signature is almost equal, suggesting more a reshuffling in the genetic expression during aging in the most ancient genes.

The AgeMeta aging signature is dominated by downregulated genes in the 'All living organisms' strata. Upregulated genes were more important in the most ancient genes in immune and ovarian cells, but not in HPC, senescent or skin cells where downregulated genes dominated in the most ancient genes. For the other types of cells, it is almost equal between up-and downregulated genes in the most ancient genes category.

Therefore, our analyses suggests that aging involves not merely a stochastic decay but a heterogeneous cellular phylogenetic dissociation during time.

4 Discussion

We tested predictions of the Atavistic Gene Expression Dissociation (AGED) hypothesis during aging using a meta-phylostratigraphic analysis. We applied it to RNA-seq and scRNA-seq data from 8 different studies two meta-analyses including different tissues RNA-seq during aging [51, 52], scRNA-seq data from skin cells [53], an aging meta-analysis of the scRNA-seq of senescent cells[54], and brain (cortex, hippocampus and cerebellum cells)[55], immune [56], ovarian [57] and stem cells RNA-seq [58] (see Table 1). We found (1) An atavistic over-representation of differential expression in the most ancient genes for two multi-tissues aging signatures, skin, ovarian, immune, senescent and mesenchymal-senescent cells; (2) No atavistic over-representation of the differential genet expression during aging of brain cells and mesenchymal stem cells; and (3) overall age-dependent increase of heterogeneity in the direction of the phylogenetic position of tissues' transcriptional profiles. Our analyses suggest that aging involves uncoordinated and tissue-specific phylogenetic changes in gene expression, revealing a cellular dissociation in phylogenetic space during aging resembling the atavistic theory of cancer for aged cells and some tissue. We also found some genetic heterogeneity in the directions of the genetic changes as sometimes it more upregulation of the most ancient genes that predominates and sometimes it is the opposite, and some cells seems not affected by this atavistic changes (brain and mesenchymal stem cells).

Numerous properties (biochemical, bioelectrical, and biomechanical) are likely affected by cells' phylogenetic status; we focused on transcriptomic analysis as expressed genes provide the only known effective method to estimate the effective phylogenetic age of a given tissue. However, it will be interesting in the future to see whether for example bioelectrical states can also be used to estimate phylogenetic position (i.e., it's not all about the genes).

To analyze the DEGs in the aging cells under various conditions through phylostratigraphic analysis, we used the evolutionary ages of 19,660 human protein-coding genes as determined by Litman et al. [59]. These genes were categorized into 19 major phylostrata, as outlined by Domazet-Loso and Tautz [46]. Phylostratigraphic analysis, while providing valuable insights into the evolutionary age of genes, is subject to several limitations that impact the accuracy and consistency of its findings. One challenge is ensuring consistency in ortholog identification across different databases[59]. Litman et al. found a consensus across several databases but for some genes, uncertainty may remain [59], leading to the possibility of both false positives or negatives. Another limitation is analyzing noncoding genes. Phylostratigraphic analysis on

these genes is more challenging as a significantly lower fraction of noncoding genes can be assigned a reliable evolutionary age [59]. This discrepancy may come from the rapid divergence and lineage-specific nature of many noncoding sequences, which results in a lower likelihood of detecting homologs across distant taxa. The absence of a consistent modal value for many noncoding genes further underscores the challenge of dating their origins, necessitating reliance on statistical estimates such as the median, which may still introduce uncertainties. In this paper, we didn't analyze the evolutionary age of the non-coding genes and focused on the protein-coding ones. The majority of noncoding genes analyzed in prior studies appear prominently from the Euteleostomi phylostratigraphic age, with the largest expansion observed during the Primata age[59]. This suggests that noncoding genes likely play critical roles in lineage-specific regulatory innovations. Future research addressing noncoding genes would be valuable, providing deeper insights into their evolutionary trajectories and functional implications in various lineages, particularly within the Primata phylostratographic age, where their abundance is highest.

Senescent behavior is not restricted to proliferative arrest. Indeed, another important characteristics of senescent cells is the senescence-associated secretory phenotype (SASP), where cells secrete inflammatory cytokines, growth factors, and proteases into their environment [65]. From an atavistic point of view, cellular senescence may not be just a passive response to molecular damage but an active, evolutionarily conserved that that occurs when the controls of multicellularity fail and cells pursue their own goals [66], and that played a role in cellular interaction and adaptation to high stress conditions[67]. However, in the case of aging, this process is dysregulated and leads to a defect of tissue homeostasis and promotes chronic inflammation [65].

Heterochronic parabiosis, the surgical connection of the circulatory systems of young and old organisms, has demonstrated that aging is not irreversible but is instead highly plastic and responsive to systemic factors [68]. From the perspective of the atavistic theory of aging, the rejuvenating effects observed in heterochronic parabiosis experiments may not come from the inhibition or reduction of pro-aging factors that along with the introduction of youthful signals, but rather from the reconstitution of the multicellular integration that has been lost and reduction of cellular phylogenetic dissociation**.** If aging is a trajectory of increasing cellular atavism, where cells revert to evolutionarily ancient behaviors, then exposure to young systemic factors may act as a re-establishment of developmental/morphogenetic constraints**,** pulling aged cells back into the organizational structure of a more coherent, goal-directed system.

Cancer can be understood as the failure of the computational boundary that regulates organ-level integration in the body [69]. The cells lose multicellular integration into networks that pursue large-scale anatomical setpoints, and function more as autonomous units that treat the rest of the body as external environment, similar to their ancestral unicellular behaviors [31, 48-50]. Therefore, cancer is believed to occur due to failure of the regulatory networks that usually restrict individual-level goals and favor morphogenetic goals such as bioelectric signalling, resulting in uncontrolled cellular autonomy and proliferation [69]. This reduction of the radius of cooperation/coordination among cells, from organ-level to individual cell level, is consistent with the loss of phylogenetic age we observed across tissues with age.

In the atavistic model of cancer, cancer progression is seen as an expression of the genetic to the ancestral cellular states, which are defined by the reactivation of the genetic programs that have been inherited from the unicellular or early multicellular evolutionary stages [47,

70]. While the somatic mutation theory (SMT) has been used to explain the development of cancer as a result of sequential mutations and natural selection events within the human body [71], the atavistic model is based on the idea that ancient functionalities that were essential for early and unicellular life forms are involved in the disease. These functionalities are uncontrolled growth, lack of response to growth inhibitors and increased stress tolerance. Phylostratigraphic analysis has been used to establish that many genes associated with cancer were born during critical transitions in the evolution of life on Earth such as the rise of unicellular, eukaryotes or multicellularity [47].

Also, in the active inference framework [72-74], cells are described as having a model of themselves and the outside world [75, 76]. Maybe evolutionary stage is part of their self-model, and the transcriptional changes we see are a readout of the change of this model with age.

Atavistic dysregulation during aging suggests new avenues for longevity therapeutics: strategies should focus on restoring and reinforcing multicellular coherence, re-establishing a multi-cellular and evolutionary younger genetic expression that preserve tissue and organ integration (perhaps by stimuli that remind cells of their modern evolutionary status). In the context of aging as a loss of morphostatic information and goal-directedness [34, 35], cellular dissociation in morphogenetic space suggests that giving evolutionarily-recent information for the organism may counteract aging. We suggest this is the beginning of a roadmap that pursues healthspan and longevity by managing the processing, by cells and tissues, of information across a wide range of temporal and spatial scales.

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Conflict of interests disclosure

The Levin lab has a sponsored research agreement with Astonishing Labs, a company seeking to impact the longevity and biomedicine of aging field.

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