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Research article

Integration single-cell and bulk RNA-sequencing data to reveal senescence gene expression profiles in heart failure

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ABSTRACT

Background: Heart failure (HF) represents one of healthcare's biggest challenges. Although rarely noticed, aging is a crucial risk factor for cardiovascular disease. Our study aims to reveal aging's role in HF by integrating single-cell RNA-sequencing (scRNA-seq) and bulk RNA-sequencing databases.

Methods: We collected HF heart sample data from the Gene Expression Omnibus database and senescence gene data from CellAge. The FindCluster () package was used for cell cluster analysis. Differentially expressed genes (DEG) were identified operating the FindMarkers function. Cell activity score calculation was performed using the AUCell package. UpSetR plotted the intersection between DEGs of active cell types, bulk data DEGs, and genes associated with aging. Using the DGIdb database gene-drug interaction data, we search for potential targeted therapeutics based on common senescence genes.

Results: The scRNA-seq data revealed myocardial heterogeneity in HF tissues. A series of crucial common senescence genes were found. The senescence gene expression profile hints at an intriguing connection between monocytes and HF. After analyzing the DEGs in the bulk dataset, the DEGs in scRNA-seq, the DEGs in each active cell type, and senescence genes, we identified ten genes as common senescence genes present in HF. Correlation analysis of transcriptomics, proteomics, and ceRNA was performed to provide ideas for future studies individually. Moreover, we discovered that common senescence genes and potential therapeutic drugs interact among different cell types. Further research is needed on the expression pattern of senescence genes and molecular regulation in HF.

Conclusions: In summary, we identified the functional significance of the senescence gene in HF using integrated data. It is possible that this more profound understanding of how senescence contributes to the development of HF will aid in unraveling the mechanisms that promote the disease and provide hints for developing therapeutics.

1. Introduction

Heart failure (HF) is a complicated, heterogeneous syndrome characterized by the decreased filling of the ventricles or impaired

Abbreviations: HF, heart failure.

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blood ejection, as well as symptoms of dyspnea, fatigue, peripheral edema, and/or pulmonary edema [1]. Although rarely noticed, aging is a crucial risk factor for cardiovascular disease [2]. Even without associated systemic risk factors such as smoking, dyslipidemia, hypertension, and diabetes, intrinsic heart aging can deteriorate heart structure and function in the elderly. According to the United Nations, the sixty-five years or older population is expected to increase from 9.5% in 2020 to 16.0% by 2050 [3]. As the average human lifespan continues to increase, the prevalence of age-associated diseases, including HF, is assuming epidemic proportions [4]. In this regard, age-related HF represents one of the biggest challenges facing global healthcare today.

Although aging has long been considered to be only the passing of time (chronological aging) [5], studies have found significant differences in the rates associated with aging (biological aging) across species, individuals, and even organs [6], which suggests that biological aging may be variable and possibly modifiable. There are nine hallmark characteristics of aging: genomic instability, telomere attrition, epigenetic alterations, proteostasis loss, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and altered intercellular communication [7]. Cellular senescence refers to a stable cell cycle arrest and the irreversible loss of cell proliferative capacity [8]. It is reported that mild to moderate expression of Sirt1 retards heart aging [9]. Age-induced expression of miR-34a and inhibition of its target PNUTS play a critical role in regulating cardiac contractile function during aging [10]. Depleting H3K9me3 in adult cardiomyocytes by overexpression of KDM4D prevents and reverses permanent cell cycle exit, leading to hyperplastic growth [11]. However, the molecular mechanisms by which cellular senescence influences HF are still largely unknown.

Avelar and colleagues developed a manually curated database of 279 human genes that play a role in cellular senescence known as CellAge [12]. A significant feature of these senescence-inducing genes is that they are overexpressed in human tissues with increasing age and overlaid with anti-longevity genes. Conversely, genes inhibiting cellular senescence are associated with pro-longevity genes. It is noted that these cellular senescence genes are not expressed in a tissue-specific manner, indicating that the expression of cellular senescence genes may vary in different organs or even in diverse cell types and finally result in distinct biological functions.

Heart tissues always contain a heterogeneous population of cells, including cardiomyocytes and non-cardiomyocytes (e.g., endothelial cells, fibroblasts, smooth muscle cells, and macrophages). For precise characterization of tissue composition, two types of RNA-sequencing are commonly considered to assess gene expression: standard bulk RNA-sequencing (bulk RNA-seq) and single-cell RNA-sequencing (scRNA-seq). In standard bulk RNA-seq, the average expression level is calculated for a sample containing various cells. [13], while scRNA-Seq determines global gene expression profiles of individual cells, facilitating the identification of previously hidden heterogeneities in cell populations [14].

Therefore, our study aims to reveal the senescence gene expression profiles in HF by integrating single-cell and bulk RNA-sequencing data. To be specific, we sought to investigate the following.

1. Do senescence genes play a role in HF?
2. How does senescence address the heterogeneity of HF cells?
3. Are there any signaling pathways involved in the regulation of cellular aging genes?
4. Are there any potential drugs that may delay senescence by targeting aging genes?

2. Methods

2.1. Data collection

HF scRNA-seq dataset (GSE145154) [15]was sequenced on the HiSeq X Ten platform (GEO accession number: GPL20795). 191, 225 cells were collected from the myocardium of human patients with dilated cardiomyopathy (DCM) and ischemic cardiomyopathy (ICM). The left ventricle (lesion) and the right ventricle (mild lesion) of DCM hearts were dissected, whereas the infarcted and non-infarcted areas of ICM hearts were dissected.

The Bulk RNA-seq set (GSE141910) was sequenced on an Illumina HiSeq 4000 platform (GEO accession number: GPL16791), containing 366 samples, including 200 HF samples and 166 non-HF samples.

The scRNA-seq and bulk RNA-seq datasets were downloaded from the Gene Expression Omnibus (GEO) (https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi).

Cellular senescence-related genes were downloaded from CellAge [12].

2.2. Single-cell sequencing data analysis

For the GSE145154 dataset, cells were discarded according to the following criteria [16,17].

1. Cells with less than 500 genes (unique molecular identifiers (UMI) > 0)
2. Cells with UMI <800 or >8000

2.3. Cells with more than 10% of mitochondrial UMI counts

After the quality control described above, the integration workflow recommended by Seurat was followed. Principal component analysis (PCA) was performed with the *RunPCA* function, and the number of the principal components (PCs) was selected using a visual graph with the *ElbowPlot* function. The *FindNeighbors* function was used to construct a shared nearest neighbor (SNN) graph for the top 30 PCs, and the *FindClusters* function with a resolution $= 0.5$ was carried out to cluster the cells. And then, the *FindAllMarkers* function

was conducted to detect the marker genes of each cluster. Differentially expressed genes (DEG) were identified by operating the *FindMarkers* function with the default parameter of the *MAST* method. The SingleR package was utilized to annotate cell types with default parameters for single-cell subsets based on the annotation information BlueprintEncodeData.

2.4. Bulk-RNA seq data differential expression analysis

Based on the GSE141910 dataset, DEG between HF and control samples (non-HF) were analyzed using the limma package. The

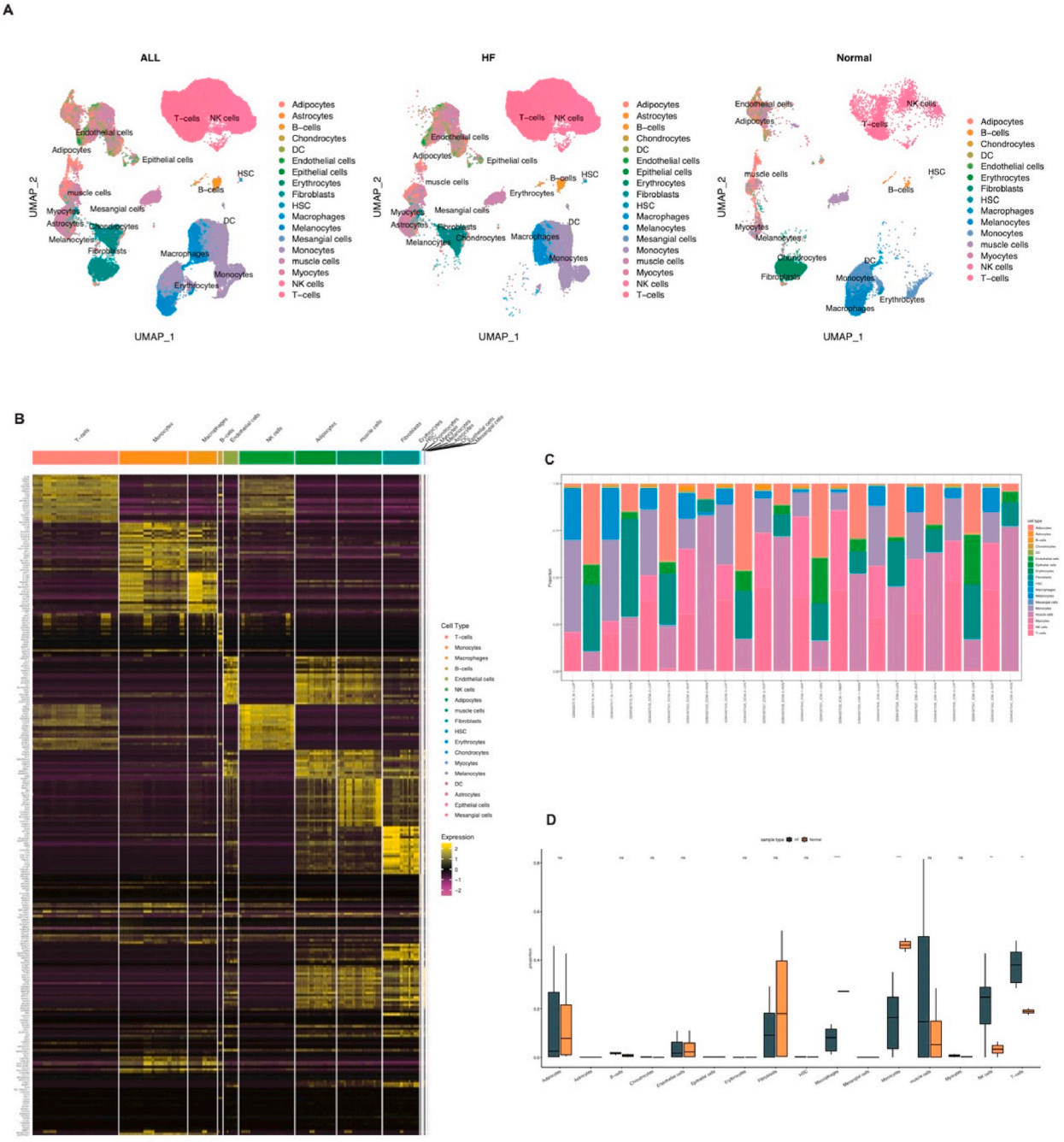

Fig. 1. Cellular heterogeneity in heart failure. A. Single-cell type annotation: all cells cell annotation (left), heart failure sample annotation (middle), normal sample annotation (right). B. Heat map of differentially expressed genes between different cell types. C. Distribution of the percentage of different cell types between different samples. D. Differences in the percentage of different cell types between normal and heart failure samples.

analysis was performed using the default parameters of the *limma* package function. Differentially expressed genes were those with adj. p.val<0.01 and |logFC|>0.585.

2.5. Active cell identification

Based on single-cell transcriptome data, cell senescence genes and cell cluster differential genes were selected to take the intersection as cell senescence DEG and cell activity score calculation was performed using the *AUCell* package.

The intersection between active cell type differential genes, bulk data differential genes, and senescence genes and their transcription factors were plotted by the *UpSetR* package.

2.6. Enrichment analysis

Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis were applied using the *clusterProfiler* package (ver. 3.9.2) after converting gene symbols to Entrez gene IDs.

2.6.1. PPI network analysis

A protein-protein interaction (PPI) construction based on STRING was further analyzed using the Cytoscape software to visualize and analyze the network. The PPI network excluded independent nodes that were not associated with other nodes. Critical nodes in the PPI network were analyzed using cytoHubba, and the threshold was taken as the top 10 nodes in degree rank.

2.7. ceRNA network construction

Based on the DEG list in the bulk RNA seq and the human genome annotation information (http://ftp.ensembl.org/pub/grch37/release-100/gtf/homo_sapiens/Homo_sapiens.GRCh37.87.gtf.gz), the differentially expressed genes were distinguished into differentially expressed mRNAs (DEmRNAs) and differentially expressed lncRNAs (DElncRNAs).

Next, we explored target miRNAs of lncRNAs, and then the databases of MiRDB and TargetScan merged DEmRNAs and differentially expressed miRNAs (DEmiRNAs). Subsequently, we integrated the interaction between DEmiRNAs and DElncRNAs or DEmRNAs to construct a ceRNA regulatory network. Cytoscape was used to visualize the ceRNA network.

2.8. Potential targeted drug prediction

Using the DGIdb database gene-drug interaction data, we search for potential targeted therapeutics based on common senescence genes. Drugs were excluded from chemotherapy drugs.

2.9. Statistics

The analysis was performed based on R4.1.3. Differences in cell type proportions were analyzed using a *t*-test. Significance was marked as ns: $p > 0.05$; *: $p \leq 0.05$; **: $p \leq 0.01$; ***: $p \leq 0.001$; ****: $p \leq 0.0001$.

3. Results

3.1. Single-cell transcriptome reveals myocardial heterogeneity in HF

After normalizing and merging the GSE145154 dataset, cells were clustered using Seurat. The results showed that the cells could be bunched into 24 clusters (Supplementary Figure S1). Specifically, based on the annotation information BlueprintEncodeData, we divided the entire cell population into small groups with similar cell states using the R package singleR. These clusters were annotated into 18 cell sorts (Fig. 1A, Figure S1). We further compared the cell type differences in mild lesions with the culprit lesions in DCM and ICM hearts. Surprisingly, epithelial and mesangial cells were missing in the mild lesion myocardium (Fig. 1A).

Next, we analyzed the DEG between different cell types and noticed significantly different expression patterns between the populations (Fig. 1B). The cell types for each sample differed immensely from sample to sample (Fig. 1C). Therefore, there was significant cellular heterogeneity in the heart failure samples. Moreover, in the mild (marked as normal) and the culprit lesions in DCM and ICM hearts (marked as HF samples), we counted the proportion of different cell types between different samples. In the HF samples, monocytes and macrophages were significantly decreased, while NK cells and T cells were remarkably increased. (Fig. 1D).

3.2. Single-cell transcriptome resolves dysregulation of cellular senescence genes

A total of 7811 differential genes between cell types were identified from the Sc-RNA sequencing (GSE145154 dataset) (Supplementary Tab. S1). As the cell senescence DEG, we intersected the cell cluster differential genes with the 279 senescence gene sets obtained from the CellAge database (Supplementary Tab. S2). Eighty-five differential expression cell senescence genes were obtained for further analysis, including 49 senescence-induce genes, 35 senescence-inhibit genes, and one with an unclear effect (Supplementary Tab. S3). The top 5 cell expression genes of the cell senescence DEGs displayed according to LogFC ranking between normal

and HF samples were TXNIP, IGFBP5, IGFBP3, AGT, and CAV1. They are senescence-induced genes highly expressed in heart failure samples compared to the normal controls (Fig. 2A). Further, dug inside the individual cell type, the top 5 cell expression genes were TNXIP in B cells, TNXIP in T cells, IGFBP5 in Fibroblasts, TNXIP in NK cells, and IGFBP3 in Fibroblasts.

Subsequently, the activity scores of cells were calculated using AUCell. Based on the AUCell, we specified 398 cells with cell senescence DEG activity (Fig. 2B). These 398 active cells were distributed among Adipocytes, Endothelial cells, Fibroblasts, Monocytes, muscle cells, and Myocytes (Fig. 2C).

Since Monocytes had significant comparative differences between normal and heart failure samples, as mentioned above, GO and KEGG enrichment analysis were conducted to discover monocyte's differentially expressed genes in normal and HF myocardium (Fig. 2D).

The results showed that the DEGs of monocytes were significantly enriched in lipid and atherosclerosis, lysosome, pertussis, and other disease-related pathways. It was suggested that the gene expression profile of monocytes might play a role in the development of HF.

3.3. Bulk RNA-sequencing analysis of HF gene expression characteristics

We analyzed the bulk sequencing data GSE141910 dataset to distinguish the differentially expressed genes between HF and non-HF samples by limma. With a threshold value of adj. $p < 0.05$, we obtained 2552 DEGs (Supplementary Tab. S4). To further investigate these DEGs, 29 senescence genes were included. They were ALOX15B, BCL6, CCND1, CDKN1A, CDKN2A, CENPA, CPEB1, DHCR24, EHF, EPHA3, ERRFI1, HJURP, HK3, IRF7, MAP2K6, MAP3K6, MATK, MMP9, MYC, PDZD2, PIK3R5, PIK3C2A, PIM1, SERPINE1, SGK1, TNFSF15, TP63, XAF1, and WWP1. (Fig. 3A, C).

Following, PCA was performed based on these 29 differentially expressed senescence genes. HF and non-HF groups were well clustered in the space, suggesting each group had distinctive expression patterns of senescence (Fig. 3B).

GO and KEGG enrichment analyses were performed to explore the potential biological function of 2552 common DEGs. In the present study, the DEGs were primarily enriched in leukocyte cell-cell adhesion (BP) (Monocytes, Supplementary Figure S2D), collagen-containing extracellular matrix (CC) (Adipocytes, Figure S2A), endoplasmic reticulum lumen (CC) (Fibroblasts, Supplementary Figure S2C), glycosaminoglycan binding (MF) (Adipocytes, Supplementary Figure S2A), Phagosome (KEGG) (Monocytes, Supplementary Figure S2D) and other pathways (Fig. 3D). A similar enrichment was observed in the single-cell analysis of senescence-

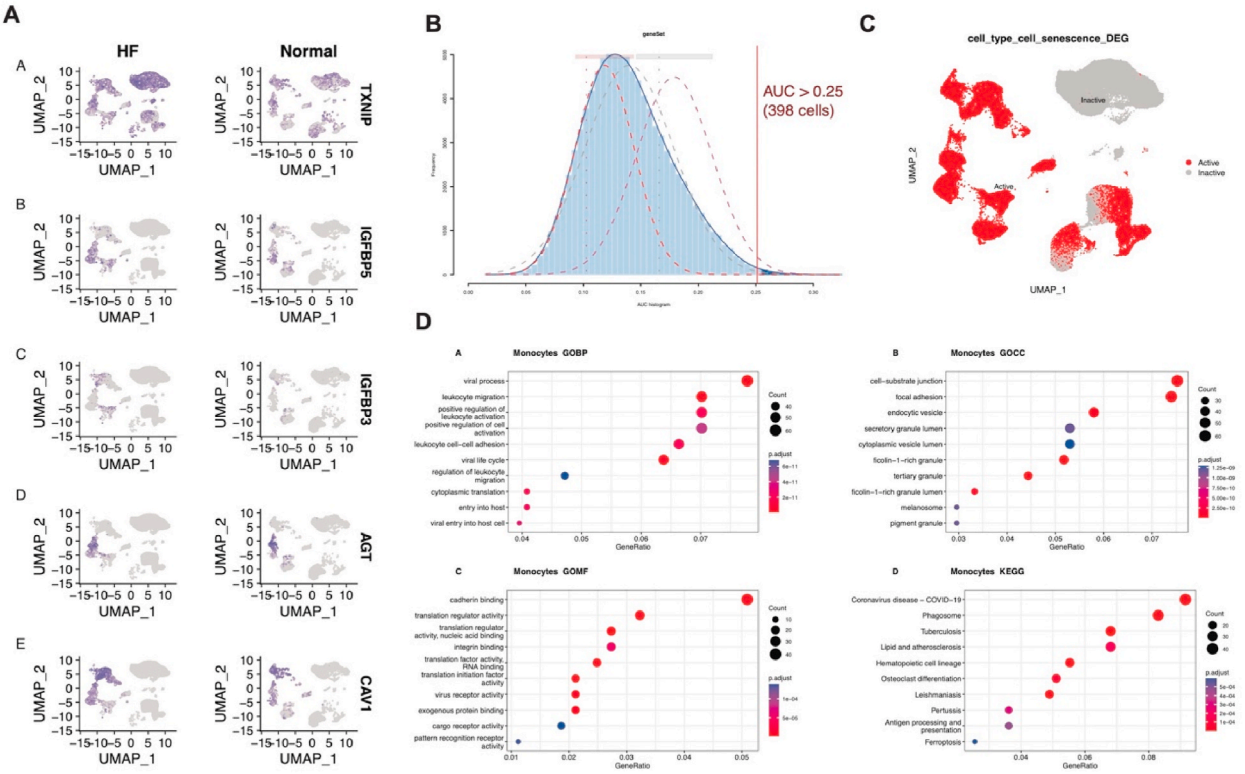

Fig. 2. Dysregulation of cellular senescence genes at the single-cell level in heart failure. A. Demonstration of top 5 DEGs (A_A.TXNIP, A_B. IGFBP5, A_C. IGFBP3, A_D. AGT, A_E.CAV1) between different cell types in normal and heart failure samples. B. Optimal thresholds for AUCell. C. Distribution of active cell types among all single-cell subpopulations. D. The GO analysis (D_A. GOBP analysis, D_B. GOCC analysis, D_C. GOMF analysis) and KEGG enrichment analysis (D_D) of differentially expressed genes in monocytes.

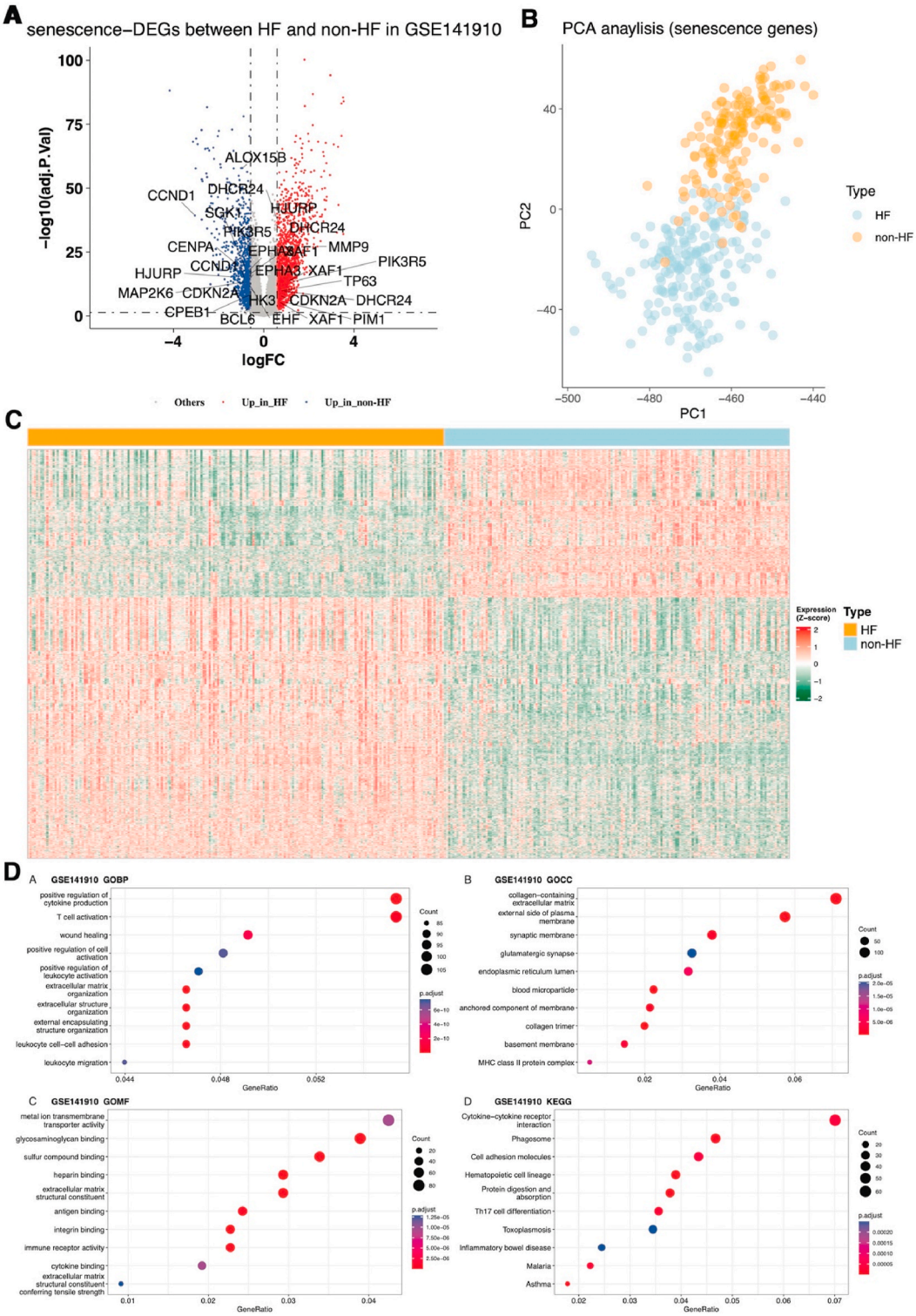

Fig. 3. Expression characteristics of HF genes in Bulk RNA-sequencing. A. Volcano plot of DEGs. Differentially expressed senescence genes are marked. B. PCA analysis based on differentially expressed senescence genes. C. Heat map of DEGs expression in HF and non-HF samples. D. The GO analysis (D_A. GOBP analysis, D_B. GOCC analysis, D_C. GOMF analysis) and KEGG enrichment analysis (D_D) of differentially expressed genes.

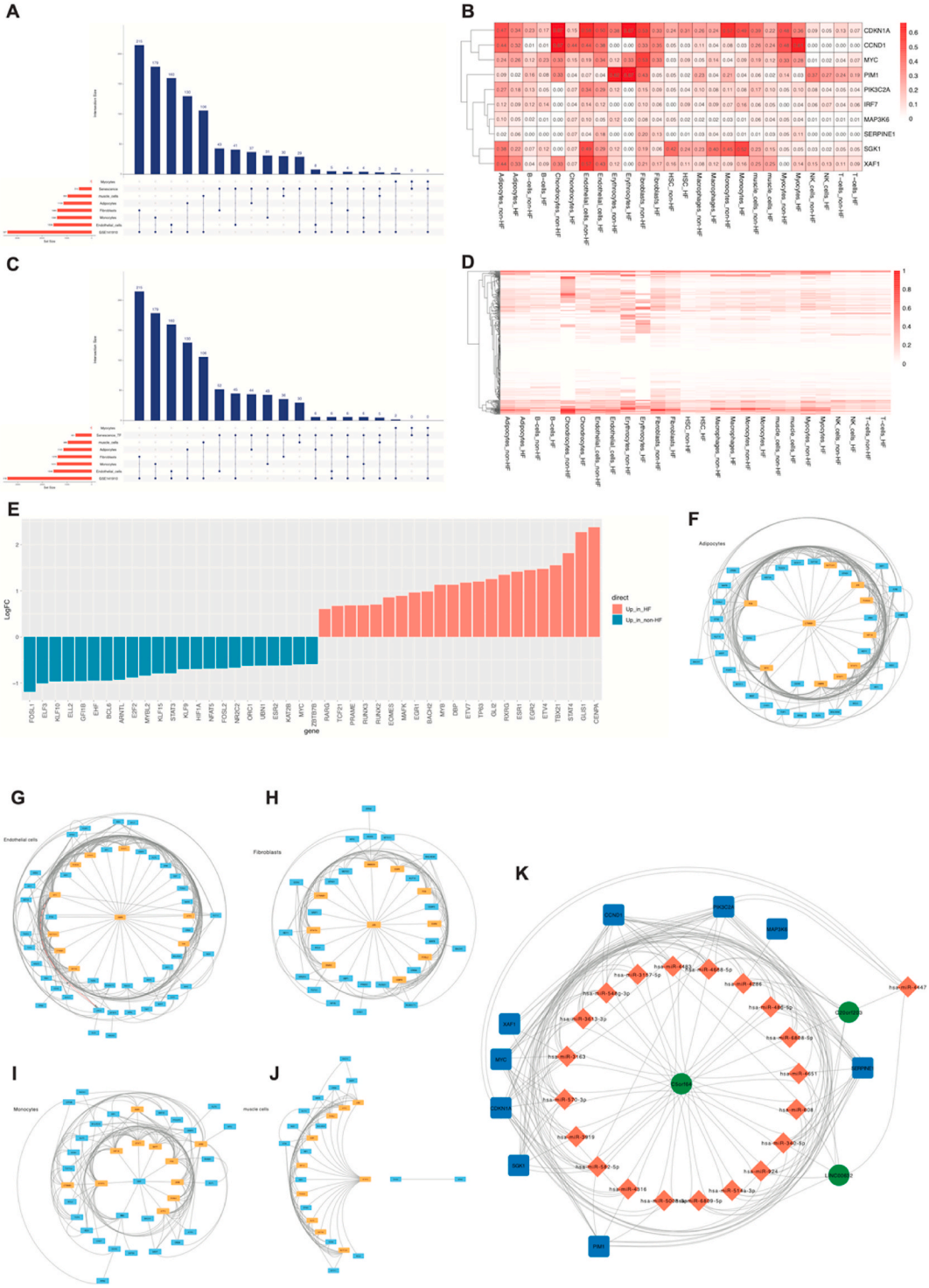

Fig. 4. Common cellular senescence gene expression characteristics and regulatory networks. A. Inclusion relationships among senescence genes, active cell types, and bulk data. B. Heat map of common senescence gene expression between different cell types. Numbers are relative expressions between HF and non-HF samples. C. Inclusion relationship of common senescence gene transcription factors in different cell types, bulk data. D. Heat map of transcription factor expression between different cell types. E. LOGFC statistics of differentially expressed senescence gene transcription factors in bulk data. F-J. PPI network of transcription factors in active cell populations. Key nodes are marked in yellow. Blue is the common node. K. ceRNA network of common senescence genes. miRNAs in red, common senescence genes in blue. Green is DElncRNA.

active cells, Monocytes (Supplementary Figure S2D), Adipocytes (Supplementary Figure S2A), and Fibroblasts (Supplementary Figure S2C).

3.4. Gene expression characteristics of common cell senescence and its regulatory network

After analyzing the DEGs in the bulk dataset, the DEGs in each active cell type, and the senescence genes, the inclusion relationship was analyzed (Fig. 4A). We identified ten as senescence genes present in bulk and on all active cell types. The genes involved were CCND1, CDKN1A, IRF7, MAP3K6, MYC, PIK3C2A, PIM1, SERPINE1, SGK1, and XAF1. Fig. 4B illustrates their differential expression between different cell subpopulations. These ten genes were expressed differently in the scRNA sequencing (GSE145154 dataset) mentioned above.

Next, transcription factors for common senescence genes were obtained from HumanTFDB and intersected with DEGs from active cells and bulk RNA sequencing. This step aimed to determine which transcription factors were specific to active cell types. By first analyzing their inclusion relationship (Fig. 4C), 372 transcription factors for senescence genes (Supplementary Tab. S5) were identified. Their expression among different cell subpopulations is shown in Fig. 4D. Our bulk analysis revealed 45 transcription factors to be differentially expressed among the DEGs (Supplementary Tab. S6, Fig. 4E).

We distinguished active cell types and constructed a PPI network between crucial transcription factors of active cell types (Fig. 4F–J). The critical node factors in the PPI network are highlighted in yellow.

Finally, we tended to construct the ceRNA network of these senescence genes. First, DEmRNAs and DElncRNAs were identified by using bulk data. By searching public databases, we predicted the upstream target miRNAs of these DEmRNAs and DElncRNAs. Based on information on the common senescence genes, their upstream miRNAs, and DElncRNAs, we constructed the ceRNA network (Fig. 4K). The ceRNA network contains 21 miRNAs, 3 DElncRNAs, and nine common senescence genes (Supplementary Tab. S7).

3.5. Potential drugs targeting common senescence genes

The DGIdb database gene-drug interactions were used for common senescence genes to identify potential therapeutic drugs. We excluded chemotherapeutic drugs from the DGIdb database (chemotherapeutic drugs are not considered for the treatment of heart failure) and then identified promising interaction relationships between 21 drugs (Azacitidine, Bortezomib, Carboplatin, Cisplatin, Cladribine, Cyclosporine, Fluorouracil, Ibrutinib, Imatinib, Indomethacin, Melphalan, Methotrexate, Methylprednisolone, Mitoxantrone, Olaparib, Paclitaxel, Palbociclib, Sirolimus, Thioguanine, Vinblastine, and Vorinostat) and four common senescence genes (CCND1, CDKN1A, MYC, PIM1). No potential target drugs exist for endothelial cells' corresponding common senescence genes. Fig. 5 shows potential drugs targeting the senescence genes for different cell types (adipocytes, fibroblasts, monocytes, and muscle cells) on the four common senescence genes. In addition, we included key transcription factors in the analysis (Figure S3).

4. Discussion

There is a strong association between aging and chronic diseases, metabolic dysfunction, multimorbidity, and geriatric syndromes. Although aging is inevitable, it is now possible to target the underlying mechanisms of aging, delay age-related functional decline, and even reduce the morbidity and mortality of chronic diseases through dietary interventions, genetic manipulation, and pharmaceutical

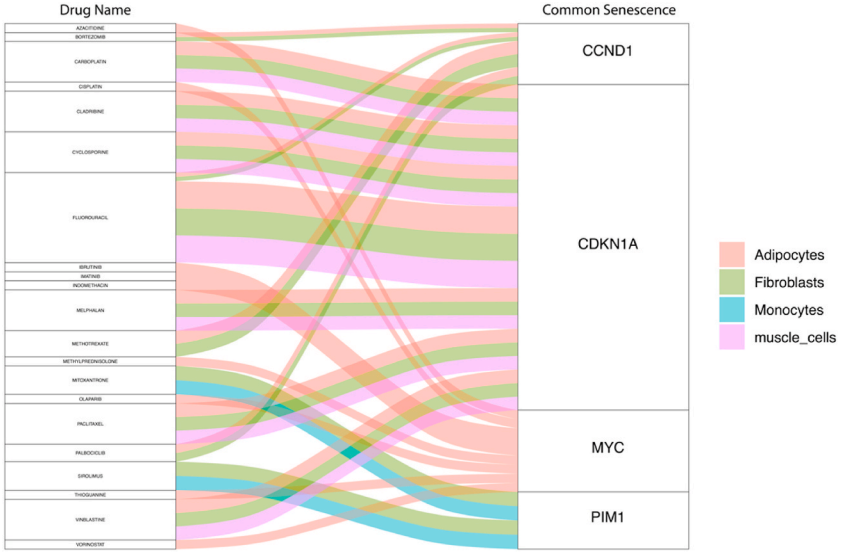

Fig. 5. Potential target drugs for common senescence genes. The different color flows represent different active cell types.

interventions.

To provide detailed insight into HF, we sought to identify gene expression patterns associated with senescence that were enriched in next-generation sequencing datasets in this study. Apart from showing a substantial overlap of regulated genes, we also analyzed the expression of cellular senescence-related genes in heart failure tissues per cell type in two datasets. Our study showed a heterogenous cell type pattern in all non-HF and HF samples. The scRNA-seq data revealed that the proportion of monocytes and macrophages was significantly decreased, while the ratio of NK cells and T cells was remarkably increased in HF tissues. This result ties nicely with previous studies wherein Laroumanie demonstrated that HF was associated with the infiltration of T cells into cardiac tissue [18]. It was also reported that there was a significant increase in the percentage of circulating monocytes to T cells in heart failure patients [19]. A high monocyte-to-T cell ratio has also been associated with severe coronary artery disease and poor clinical outcomes in patients with non-ST-elevation myocardial infarction and heart failure [20]. According to these factors, immune cells may be a critical contributor to the pathological development of heart failure.

We cross-referenced the differential genes between the cell clusters and the 279 senescence gene sets obtained from the CellAge database to investigate the relationship between HF and cell senescence. A total of 49 senescence-inducing genes and 35 senescence-inhibiting genes were found. Notably, in human heart failure samples, TNXIP is upregulated in almost all cell types, especially immune cells (B cells, T cells, and NK cells) (Supplement Tab. S3). According to Yoshioka J [21], TXNIP-KO hearts enhanced recovery of cardiac function after an ischemia-reperfusion insult. Cardiomyocyte-specific TXNIP deletions reduced infarct size following reversible coronary ligation. The investigators explained from the perspective of energy metabolism that knocking out TXNIP suppressed mitochondrial function. However, a boost in anaerobic metabolism helped protect against myocardial ischemia by providing energy outside mitochondria.Nevertheless, TXNIP acts as a link between redox regulation and senescence pathogenesis [22,23]. The expression of TXNIP may also be elevated during senescence, resulting in the characteristic senescence signs in young cells when TXNIP is upregulated [24]. In line with the previous study, we can hypothesize that TXNIP knockdown may protect against ischemia-reperfusion injury through a mechanism related to anti-aging.

In addition, we identified 398 cells with cell senescence DEG activity based on the scRNA-seq results. These 398 active cells were distributed among Adipocytes, Endothelial cells, Fibroblasts, Monocytes, muscle cells, and Myocytes. The heterogeneity of cell types expression in heart failure tissues led us to conduct GO and KEGG enrichment analyses in monocytes. We found that the DEGs of monocytes were significantly enriched in pathways related to lipid and atherosclerosis, lysosomes, pertussis, and other diseases. The senescence gene expression profile hints at an intriguing connection between monocytes and heart failure.

Another promising finding was that after analyzing the DEGs in the bulk dataset, the DEGs in scRNA-seq, the DEGs in each active cell type, and the senescence genes, we identified ten genes as senescence genes present in HF. These HF-related senescence genes were CCND1, CDKN1A, IRF7, MAP3K6, MYC, PIK3C2A, PIM1, SERPINE1, SGK1, and XAF1. A subsequent study may be able to build on the discovery of these genes.

Correlation analysis of transcriptomics, proteomics, and ceRNA was performed to provide ideas for future studies in the bulk database individually. We analyzed the bulk data's intrinsic association of transcription factors with active cells. A total of 45 transcription factors were identified in association with differential aging genes, 22 of which were highly expressed in heart failure samples. PPI networks were also constructed separately for adipocytes, endothelial cells, fibroblasts, monocytes, and myocytes to clarify the relationship between the proteins. Meanwhile, we identified a ceRNA network containing 21 miRNAs and nine common senescence genes based on three senescence-associated lncRNAs (linc00632, C5orf64, and C20orf203).

The ultimate goal of research on aging is to identify therapeutic targets to retard aging. Rapamycin can extend the average lifespan of yeast, C. *elegans*, and fruit flies by inhibiting the mTOR protein kinase pathway [25]. However, further research is needed to determine its role in mammals. Resveratrol has shown remarkable promise in multiple animal models [26,27]. Regardless, its low bioavailability precludes its use in human clinical trials [28,29]. Whether metformin increases lifespan remains controversial, despite data showing that the drug has anti-aging effects [30]. This study also identified interaction relationships between 21 drugs and four common senescence genes (CCND1, CDKN1A, MYC, PIM1) in adipocytes, fibroblasts, monocytes, and muscle cells. These promising results are to be verified in our subsequent series of studies.

However, the study had limitations. Our results are based on one sc-RNA seq and one bulk sequencing database, and the sample size is relatively small. Moreover, this study's definition of senescence genes is confined to the 279 genes in the CellAge database, which results in some consequential senescence genes that may be missed. Considering the results of this study, we will continue to validate and explore and try to conduct clinical studies to investigate the role of aging in heart failure.

5. Conclusion

In summary, the scRNA-seq data revealed myocardial heterogeneity in HF. We obtained a series of crucial common senescence genes and revealed their possible expression patterns in HF by combining the analysis results of bulk RNA-seq and scRNA-seq. The transcription factors and ceRNAs were identified. The senescence gene expression profile hints at an intriguing connection between monocytes and heart failure. Moreover, we discovered that common senescence genes and potential therapeutic drugs interact in different cell types, which could be a promising treatment option for patients with heart failure. Further studies on the senescence gene expression pattern and molecular regulation in HF are required to validate our findings.

A preprint has previously been published [31].

Availability of data and materials

The HF scRNA-seq dataset and the Bulk RNA-seq dataset analyzed in this research can be found at:https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi. Cellular senescence-related genes were downloaded from: https://genomics.senescence.info/cells/. The human genome annotation information was gained from http://ftp.ensembl.org/pub/grch37/release-100/gtf/homo_sapiens/Homo_sapiens.GRCh37.87.gtf.gz.

Author contribution statement

Zheng Kuai:performed the experiments, analyzed, and interpreted the data and wrote the paper.

Yu Hu:conceived and designed the experiments, contributed reagents, materials, analysis tools or data and final approval of the version submitted.

Data availability statement

Data included in article/supp. material/referenced in article.

Additional information

No additional information is available for this paper.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Abbreviations

HF	Heart failure
scRNA-seq	single cell RNA-sequencing
DEG	Differentially expressed genes
bulk RNA-seq	bulk RNA-sequencing
DCM	dilated cardiomyopathy
ICM	ischemic cardiomyopathy
GEO	Gene Expression Omnibus
PCA	Principal component analysis
PCs	principal components
SNN	shared nearest neighbor
GO	Gene Ontology
KEGG	Kyoto Encyclopedia of Genes and Genomes
PPI	protein-protein interaction
DEmRNAs	differentially expressed mRNAs
DElncRNAs	differentially expressed lncRNAs
DEmiRNAs	differentially expressed miRNAs

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e16214.

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