

Transcriptomic Reprogramming in Senescence Induced Fibroblasts

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Introduction

- Senescent cells contribute to tumor suppression, tissue repair, development, and aging, but their persistence drives inflammation and tissue dysfunction via the senescence-associated secretory phenotype (SASP).
- Cellular senescence is an irreversible growth arrest induced by stressors such as ionizing radiation, involving DNA damage, p53–p21 signaling, and SASP activation.
- In contrast, quiescence is a reversible, non-damaging arrest occurring under normal conditions like nutrient deprivation.
- The Hernandez et al. RNA-seq dataset (proliferating, quiescent, and irradiated fibroblasts at days 4, 10, and 20) enables a time-resolved comparison of transcriptional changes in radiation-induced senescence versus quiescence.

Research Question

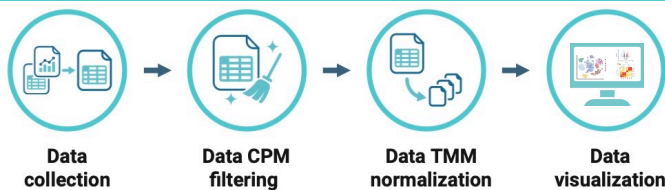
How does the transcriptomic profile of primary human foreskin fibroblasts change over time during ionizing-radiation-induced senescence (days 4, 10, and 20 post-irradiation) compared with quiescent and proliferating cells?

Hypotheses

Following ionizing radiation, fibroblasts are expected to show:

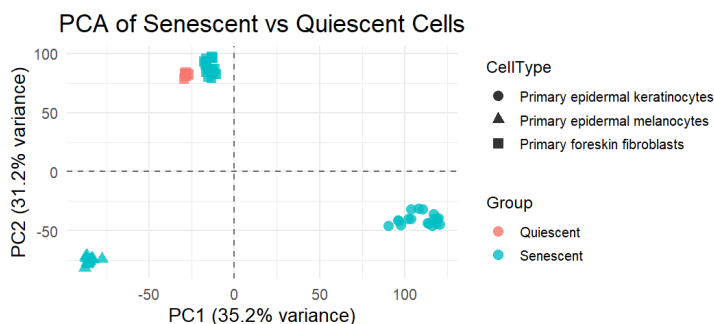
- DNA damage response and cell-cycle arrest at **day 4**
- peak SASP and inflammation at **day 10**
- stabilization of late senescence features, including ECM and chromatin remodeling, by **day 20**.

Material and Methods



Results

Figure 1: Principal Component Analysis (PCA) of quiescent and senescent cells across multiple cell types shows that quiescent cells are only present in primary foreskin fibroblasts.



Results

Figure 2: Volcano plot of differential gene expression between IR day 20 and quiescent fibroblasts, with significant upregulation of senescence- and DNA damage-related genes and downregulation of cell-cycle genes.

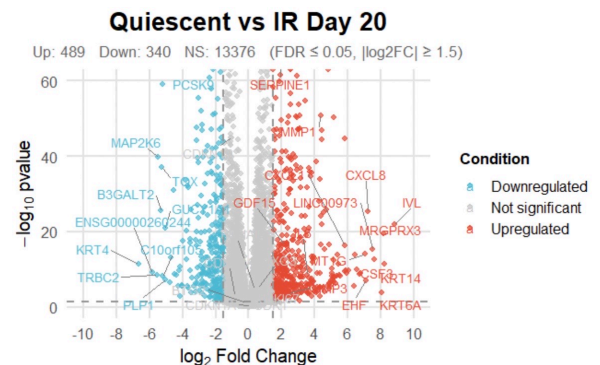
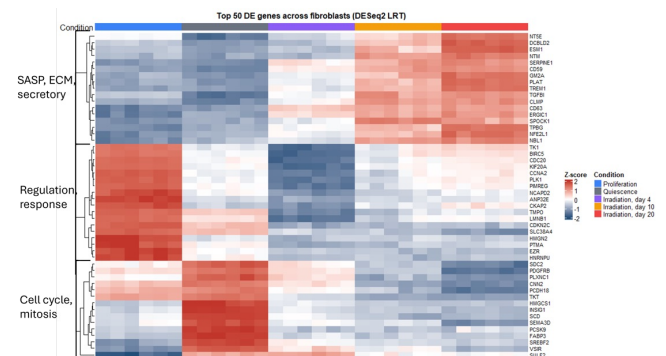


Figure 3: Heatmap of the top 50 differentially expressed genes across fibroblast conditions reveals progressive transcriptional reprogramming during irradiation-induced senescence.



Conclusion

- Quiescent cells were identified only in fibroblasts (Fig. 1), establishing them as the focus of our analyses.
- Transcriptomic data showed downregulation of cell-cycle genes and upregulation of DNA-damage and senescence pathways in quiescent fibroblasts (Fig. 2).
- Fibroblasts exhibited progressive transcriptional reprogramming from early DNA-damage response (day 4) to SASP activation and ECM remodeling (days 10–20) (Fig. 3).
- Classification effectively distinguished proliferating, quiescent, and senescent states, capturing the temporal dynamics of radiation-induced senescence.
- Together, these findings support fibroblasts as a robust model system for studying senescence at the transcriptomic level.

Future Perspective

- Extend analyses to other cell types and stressors to test fibroblast specificity.
- Apply trajectory and machine-learning models to capture transitions between cell states.
- Integrate single-cell and multi-omics data to uncover heterogeneity within senescent populations

