Systemic Senolytic Treatment with Dasatinib + Quercetin Exhibits Age-Dependent Effects on Acute Cutaneous Wound Healing

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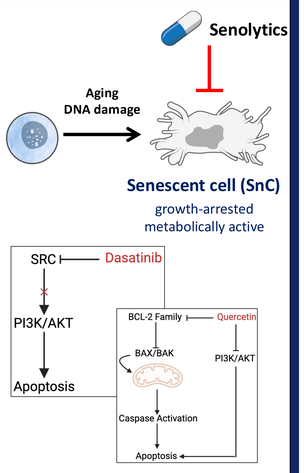
Background

SnCs impair regeneration in several organ systems, but they also play paradoxical roles in tissue repair[2,3]. This raises questions as senolytics such as Dastinib + Quercetin (D+Q) are being tested in trials for age-related diseases[4], such as osteoporosis[6], DKD[7], pulmonary fibrosis[8]. We chose to evaluate D+Q impact on wound healing, in which senolytics role is unclear.

Hypothesis:
We hypothesized that systemic senolytic therapy would have age-dependent effects, potentially disrupting beneficial acute senescence in young wounds while alleviating chronic senescence-associated dysfunction in aged wounds.



Methods

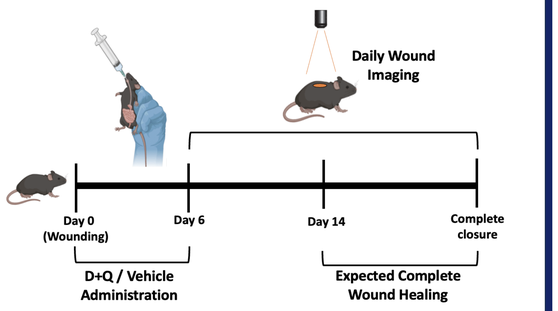


Figure 1. Experimental design. Full-thickness 10 mm excisional wounds were created in 2-month and 24-month-old mice. Animals received oral Dasatinib plus Quercetin (D+Q) or vehicle from Day 0 through Day 6. Wounds were photographed daily until complete closure. A separate cohort of young and aged mice was harvested on Day 6 for gene expression analysis and histologic evaluation.

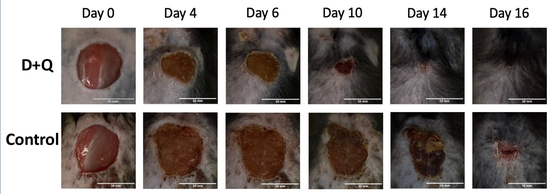


Figure 2. Representative images of wounds from D+Q and vehicle-treated aged mice. Serial photographs demonstrate accelerated wound contraction and earlier closure in D+Q-treated aged mice compared with vehicle-treated controls. Each wound area is normalized to the individual animal's Day 0 baseline to account for minor differences in initial wound size.

Wound Closure Young vs Aged

D+Q did not impair wound healing in either young or aged mice. Early wound expansion was reduced in both age groups following treatment. Notably, D+Q significantly accelerated closure in aged mice: 43% achieved complete healing by Day 16 and 86% by Day 22, compared with 0% and 57%, respectively, in vehicle-treated aged controls. The healing trajectory of D+Q-treated aged mice closely approximated that of young mice, which typically reach complete closure around Day 18.

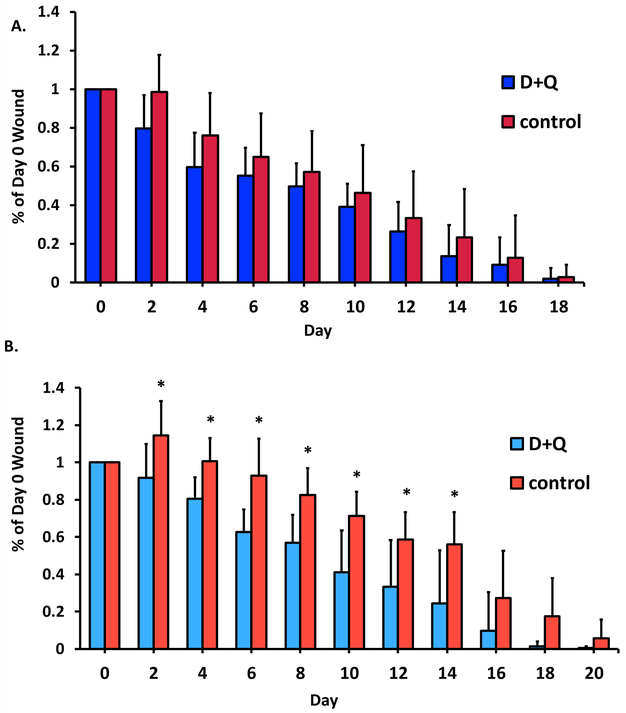


Figure 3. Age-dependent effects of D+Q on wound healing. (A) D+Q treatment (N = 10) does not impair wound closure in young mice compared with vehicle-treated controls (N = 10). (B) D+Q treatment (N = 7) accelerates wound closure in aged mice compared with vehicle-treated aged controls (N = 8). (C) A greater proportion of aged D+Q-treated mice achieved complete wound closure earlier than vehicle-treated controls (42.9% by Day 16 vs. 42.9% by Day 20). Statistical analysis was performed using multiple comparisons unpaired t-tests (Welch's correction for unequal variances) with false discovery rate correction; *q < 0.05.

Early Wound Healing Dynamics

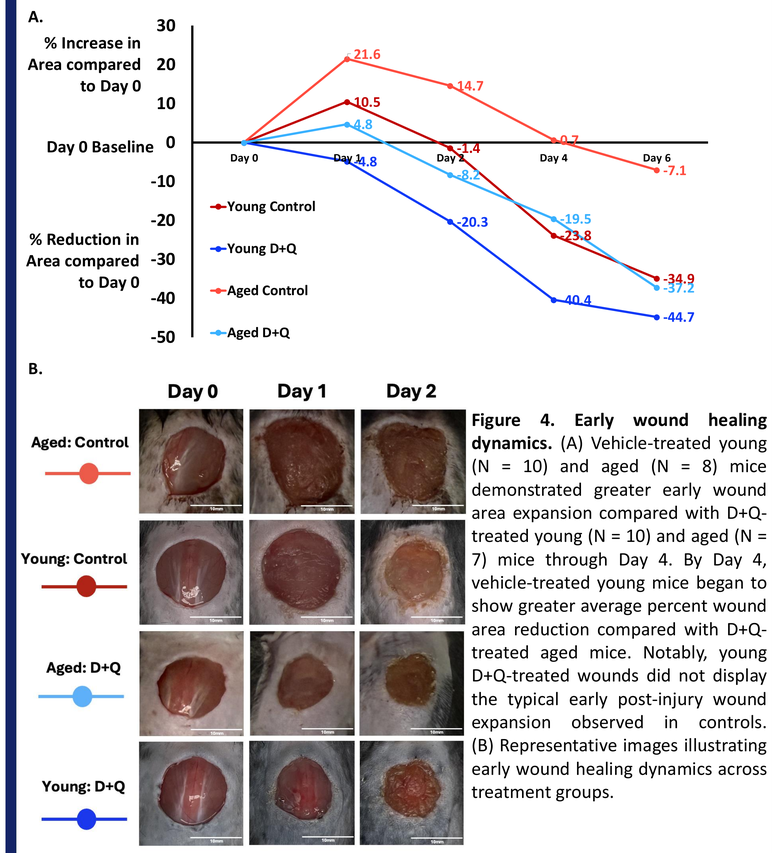


Figure 4. Early wound healing dynamics. (A) Vehicle-treated young (N = 10) and aged (N = 8) mice demonstrated greater early wound area expansion compared with D+Q-treated young (N = 10) and aged (N = 7) mice through Day 4. By Day 4, vehicle-treated young mice began to show greater average percent wound area reduction compared with D+Q-treated aged mice. Notably, young D+Q-treated wounds did not display the typical early post-injury wound expansion observed in controls. (B) Representative images illustrating early wound healing dynamics across treatment groups.

Senescence Marker Gene Expression

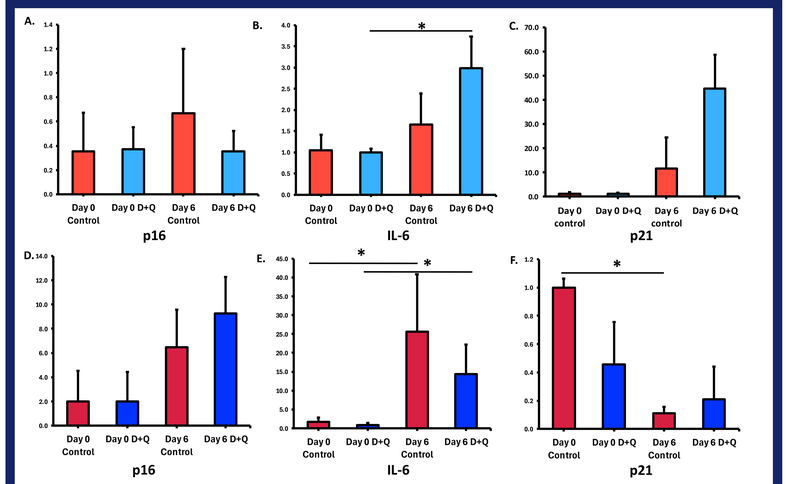


Figure 5: Preliminary results of senescence marker expression on Day 6. Relative p16, IL-6, p21 expression for aged (A-C) and young (D-F). *p<0.05, two-tailed t-test with unequal/equal variances.

Conclusions

This study demonstrates age-dependent effects of systemic senolytic therapy on cutaneous wound healing. Short-term D+Q administration does not impair acute wound repair in young mice and significantly accelerates closure in aged mice.

These findings suggest that wound senescent cell populations differ functionally with aging and may contribute differently to wound healing dynamics across the lifespan. Our results support the possibility that senolytic therapy can improve repair kinetics in aged tissue without disrupting early healing responses in young skin. Ongoing studies are evaluating whether D+Q alters senescent cell burden, inflammatory signaling, and tissue remodeling, as well as its effects on scar quality and tensile strength (Figure 6).

Collectively, these findings provide important preclinical evidence supporting the potential safety and therapeutic relevance of senolytics in surgical and wound care settings in aging populations.

Figure 6. Future perioperative model: Ex vivo studies will evaluate the effects of D+Q on incisional wound healing, with assessment of tissue repair quality and tensile strength.

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Acknowledgments

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