Early Angiopoietin-2 Elevation Identifies Immune and Coagulation Dysregulation and a Targetable Endothelial Pathway

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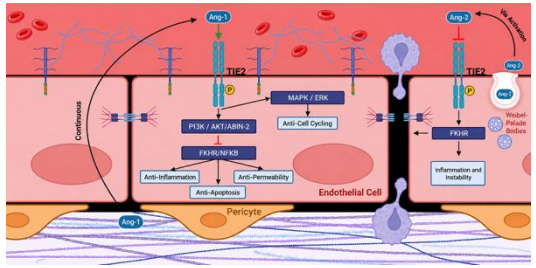
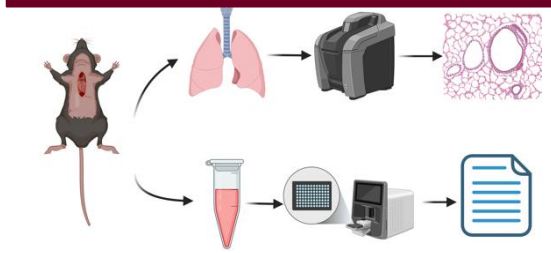
Burn injury activates an Ang-2/TIE2 endothelial-immune response. Low-dose AV-001 shows its clearest 1-day signal in plasma EGF and exploratory field-level lung morphology; qPCR and whole-lung pTIE2 remain non-definitive at this time point.

Ang-2/TIE2 after burn



Ang-2 antagonizes TIE2 and is linked to endothelial dysfunction, vascular leak, and ARDS. Early post-burn Ang-2 elevation may identify an immune-endothelial dysfunction state. We tested whether low-dose AV-001, a TIE2 agonism improves endothelial signaling and lung injury after burn.

Murine AV-001 experiment

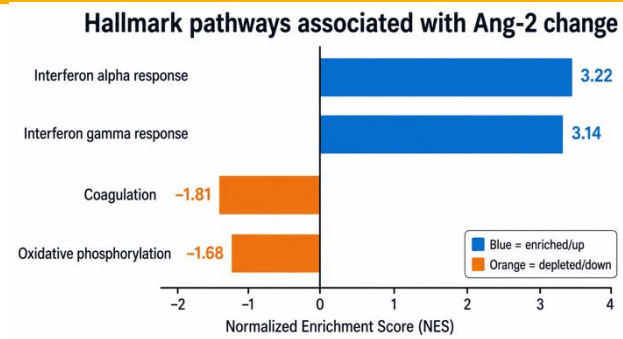


Model: male C57BL/6 mice received sham or 12.5% TBSA burn, then placebo, low-dose AV-001 (17.5 µg), or high-dose AV-001 (35 µg).

Readouts at 1-day: plasma Ang-2/EGF, lung RT-qPCR, whole-lung pTIE2, and H&E morphometry.

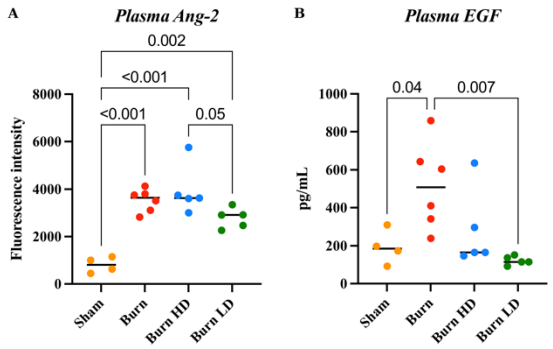
Stats: ANOVA/Tukey; qPCR on ΔCt with BH-FDR; H&E reported as field-level morphometry.

Human translational signal



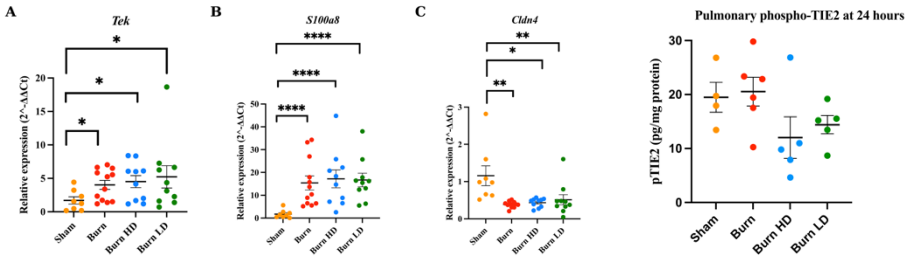
Higher Ang-2 change aligned with interferon enrichment and relative depletion of coagulation and oxidative phosphorylation pathways.

Systemic response: EGF decreases with low-dose AV-001



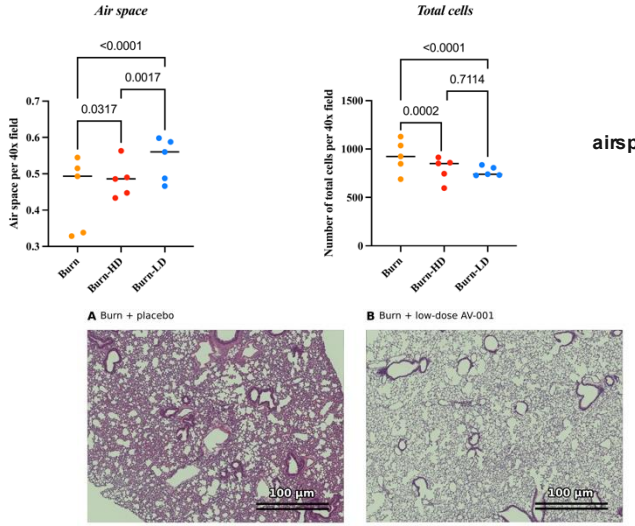
Low-dose AV-001 reduced circulating EGF vs burn placebo (p=0.007), while Ang-2 remained elevated after burn.

Lung molecular readouts



Burn increased Tek and S100a8 and lowered Cldn4 vs sham. AV-001 did not change these qPCR findings; whole-lung pTIE2 was not significant at 24 h (p=0.149).

Lung Morphometry on H&E



Burn vs low dose
field-level H&E:
airspace ↑ and total cells ↓
both p < 0.0001

Representative 40x H&E: A) burn placebo vs B) burn + low-dose AV-001.

Conclusion

Low-dose AV-001 reduced circulating EGF at 24 h. Lung qPCR and whole-lung pTIE2 were not definitive, while field-level H&E morphometry supported a favorable low-dose structural response.

References: Murray et al., Eur Burn J 2026; Khair et al., J Burn Care Res 2025; Lask et al., Sci Rep 2022.
Abbrev.: Ang-2, angiopoietin-2; EGF, epidermal growth factor; FDR, false discovery rate; H&E, hematoxylin and eosin; pTIE2, phospho-TIE2; TBSA, total body surface area.