Expanded View Figures

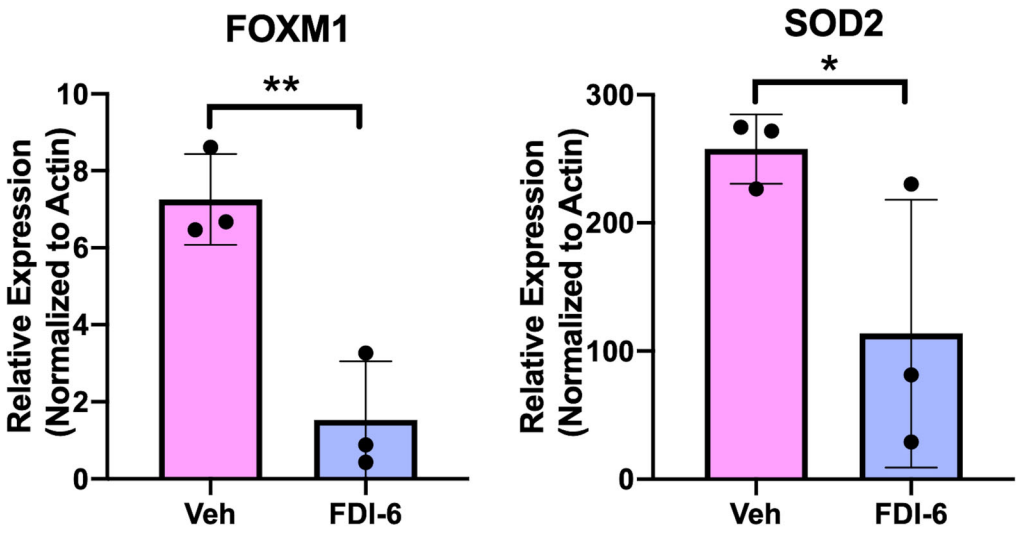


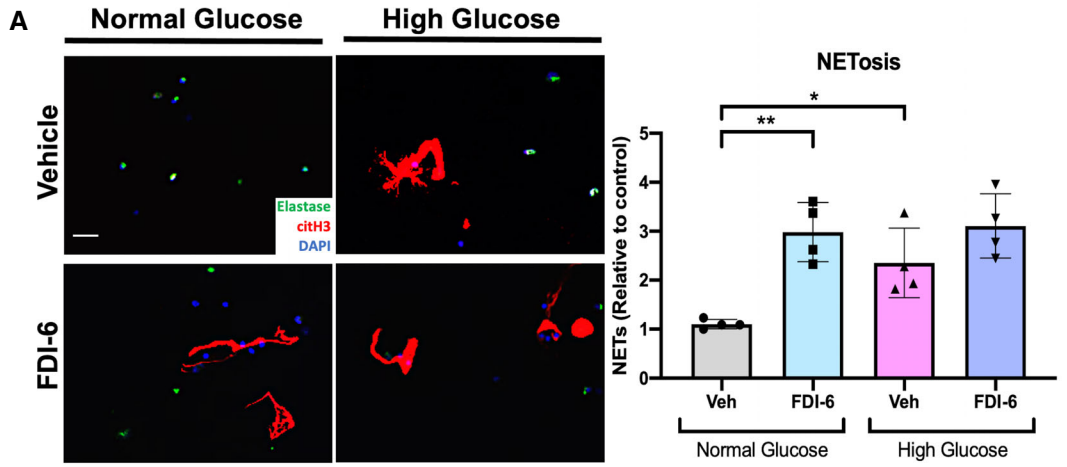
Figure EV1. Inhibition of FOXM1 with FDI-6 suppresses FOXM1 expression and downstream target genes in human neutrophils.

Human neutrophils were treated with FDI-6 for 3 h. Vehicle (DMSO) served as a control. Treatment with FDI-6 inhibits FOXM1 expression and its downstream target SOD2. $n = 3$ biological replicates. Data presented as mean ± SD. *$P < 0.05$. **$P < 0.01$ (two-tailed unpaired Student's t-test).

Figure EV2. Inhibition of FOXM1 induces NET formation *in vitro* and *in vivo*.

A Human neutrophils cultured in either normal glucose media (5 mM glucose) or high glucose media (25 mM) to recapitulate diabetic conditions and treated with FDI-6. Vehicle (DMSO) served as a control. NETs were visualized by immunostaining with citH3 and the neutrophil marker, elastase. (Scale bar: 50 μm). Quantification of $n = 4$ biological replicates per group were performed. Data presented as mean ± SD. *$P < 0.05$, and **$P < 0.01$ (one-way ANOVA followed by Sidak *post-hoc* test).

B Immunofluorescence staining of vehicle (DMSO) and FDI-6 treated wounds in STZ-induced diabetic mice at day 4 showing basal keratin marker K5, and NET marker citH3. Treatment of diabetic wounds with FDI-6 resulted in increased citH3 compared to vehicle treated wounds. (Scale bar: 50 μm). Quantification of wound areas in $n = 3$ wounds per group were performed with Fiji software. Data presented as mean ± SD. **$P < 0.01$ (one-way ANOVA followed by Sidak *post-hoc* test).



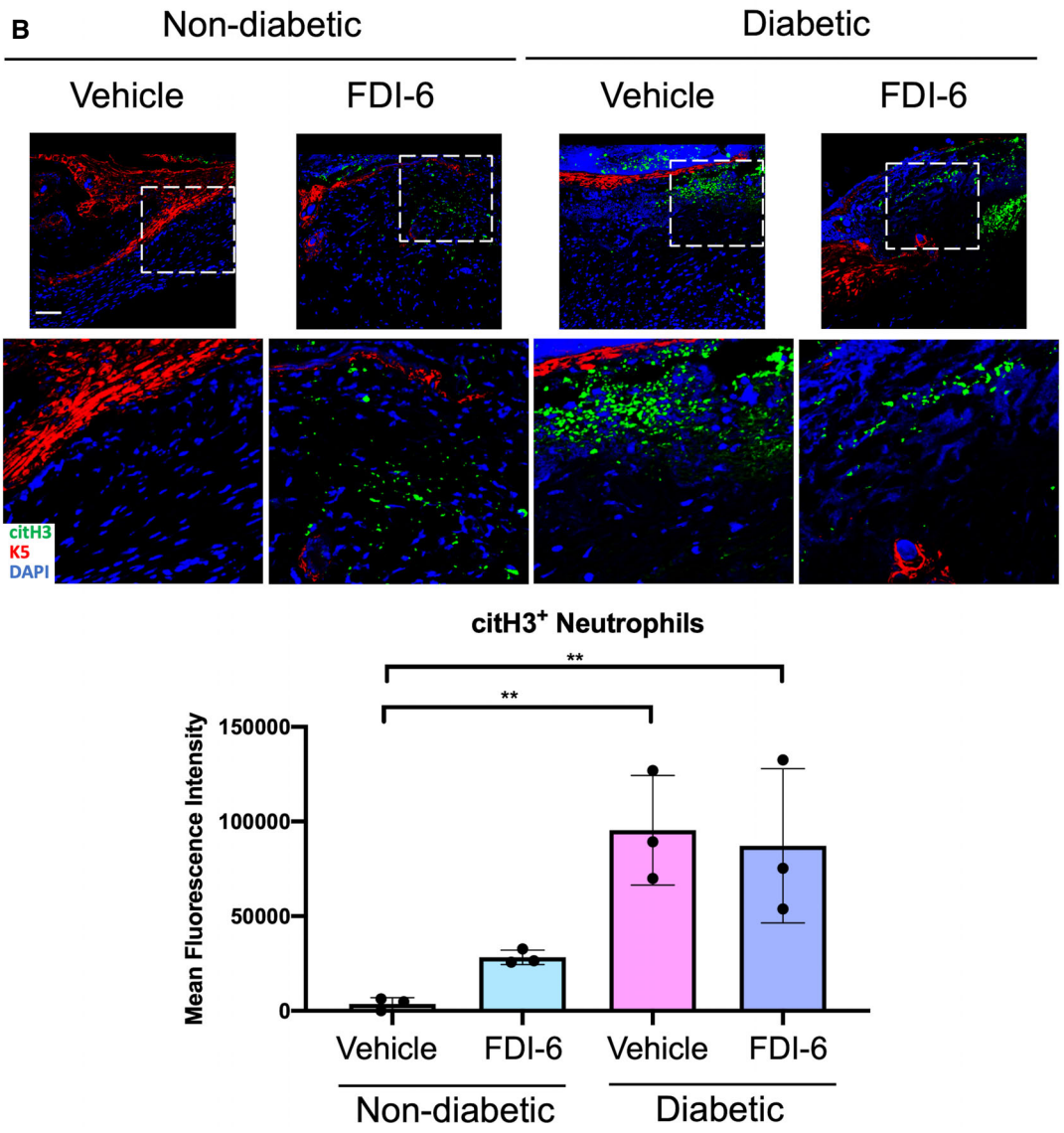


Figure EV2.

Figure EV3. FOXM1 regulates ROS levels during wound healing.

A FOXM1 regulates genes involved in reducing ROS levels and is activated in human skin acute day 3 wounds compared to suppression in human DFUs.

B Representative images of human neutrophils treated with the FOXM1 inhibitor, FDI-6, in presence or absence of NAC. PMA served as positive control. Reactive oxygen species formation are visualized in green. Representative images of human neutrophils treated with the FOXM1 inhibitor, FDI-6, in presence or absence of NAC. PMA served as positive control. NET formation are visualized in green. (Scale bar: 100 μm).

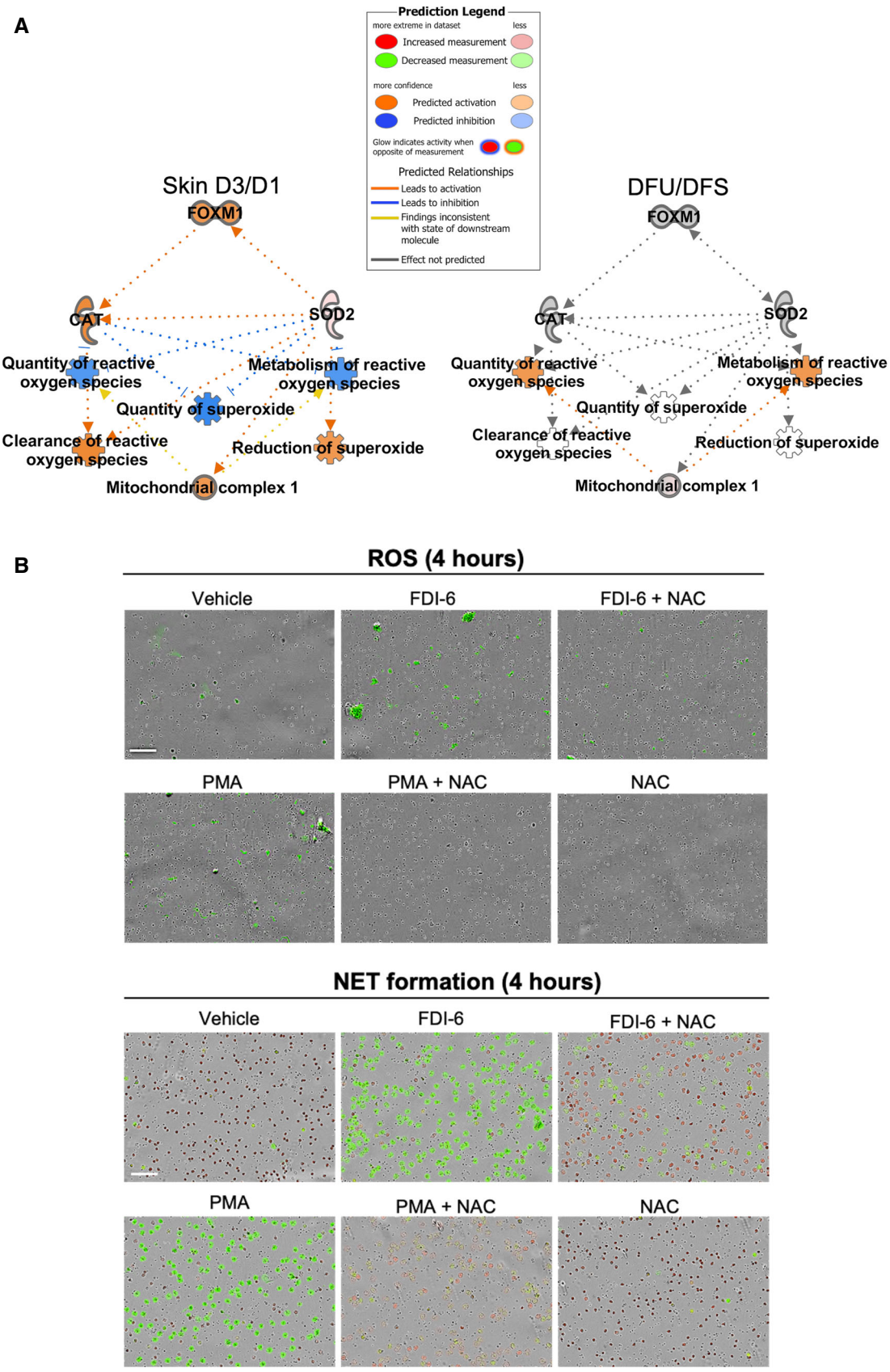
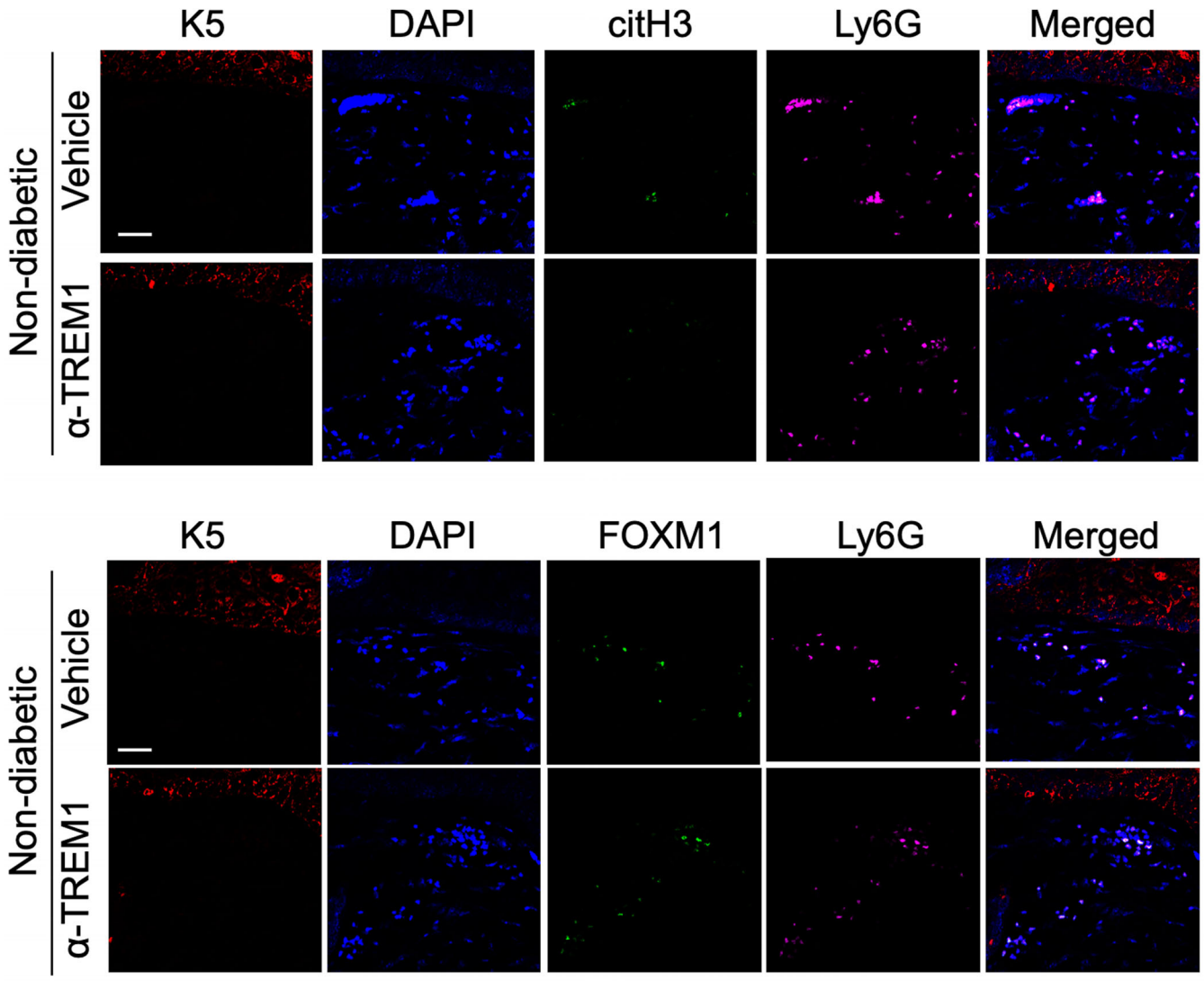


Figure EV3.

Figure EV4. Treatment with α-TREM1 has no significant effect on FOXM1 and citH3 in nondiabetic wounds.

Representative pictures of vehicle (IgG isotype control) and α-TREM1-treated nondiabetic wounds at day 4 show basal keratin marker K5, and neutrophil marker Ly6G, FOXM1, and citH3. Treatment of wounds with α-TREM1 resulted in no significant differences in $FOXM1^+$ and $citH3^+$ neutrophils compared to vehicle-treated wounds. (Scale bar: 50 μm). Quantification of mean fluorescence intensity was performed with Fiji software. $n = 3$ wounds per group. Data presented as mean ± SD (two-tailed unpaired Student's *t*-test).



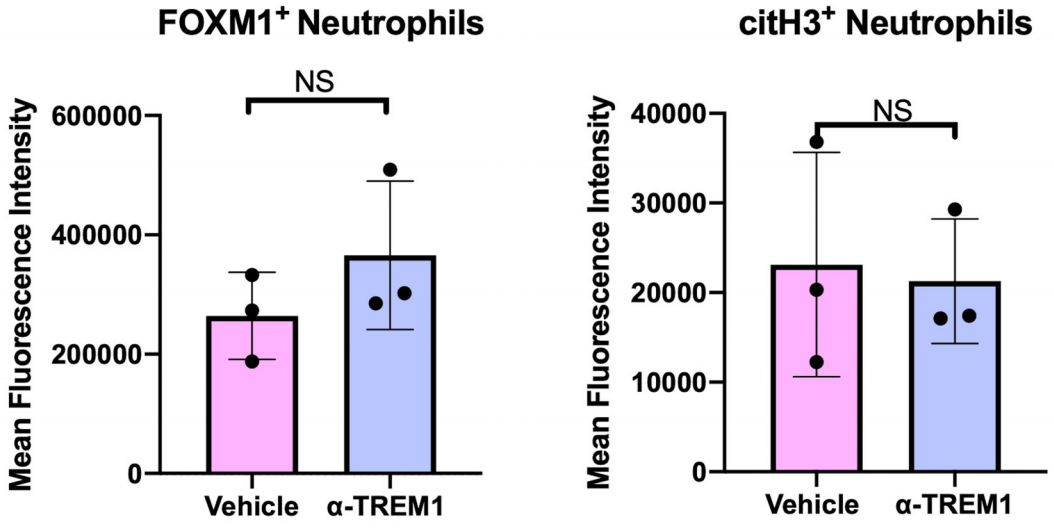


Figure EV4.