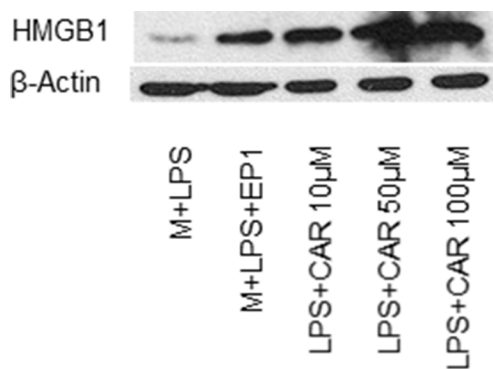
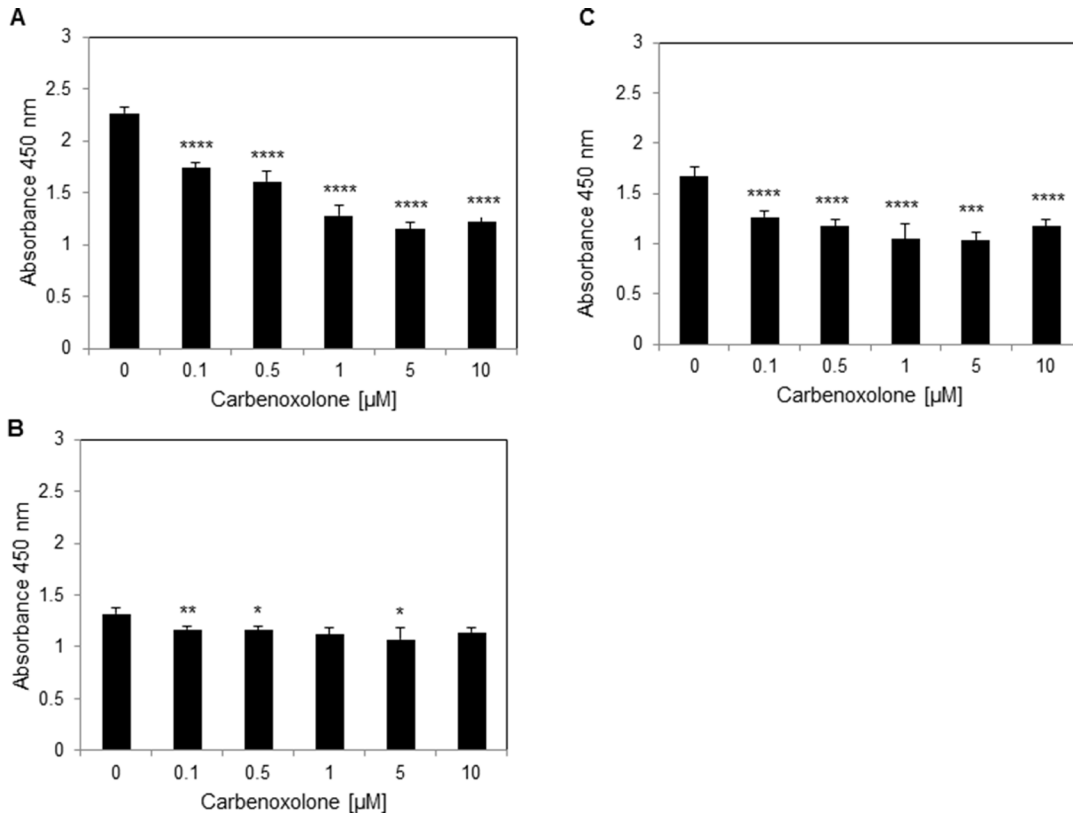


High mobility group box 1 antagonist limits metastatic seeding in the lungs via reduction of cell-cell adhesion

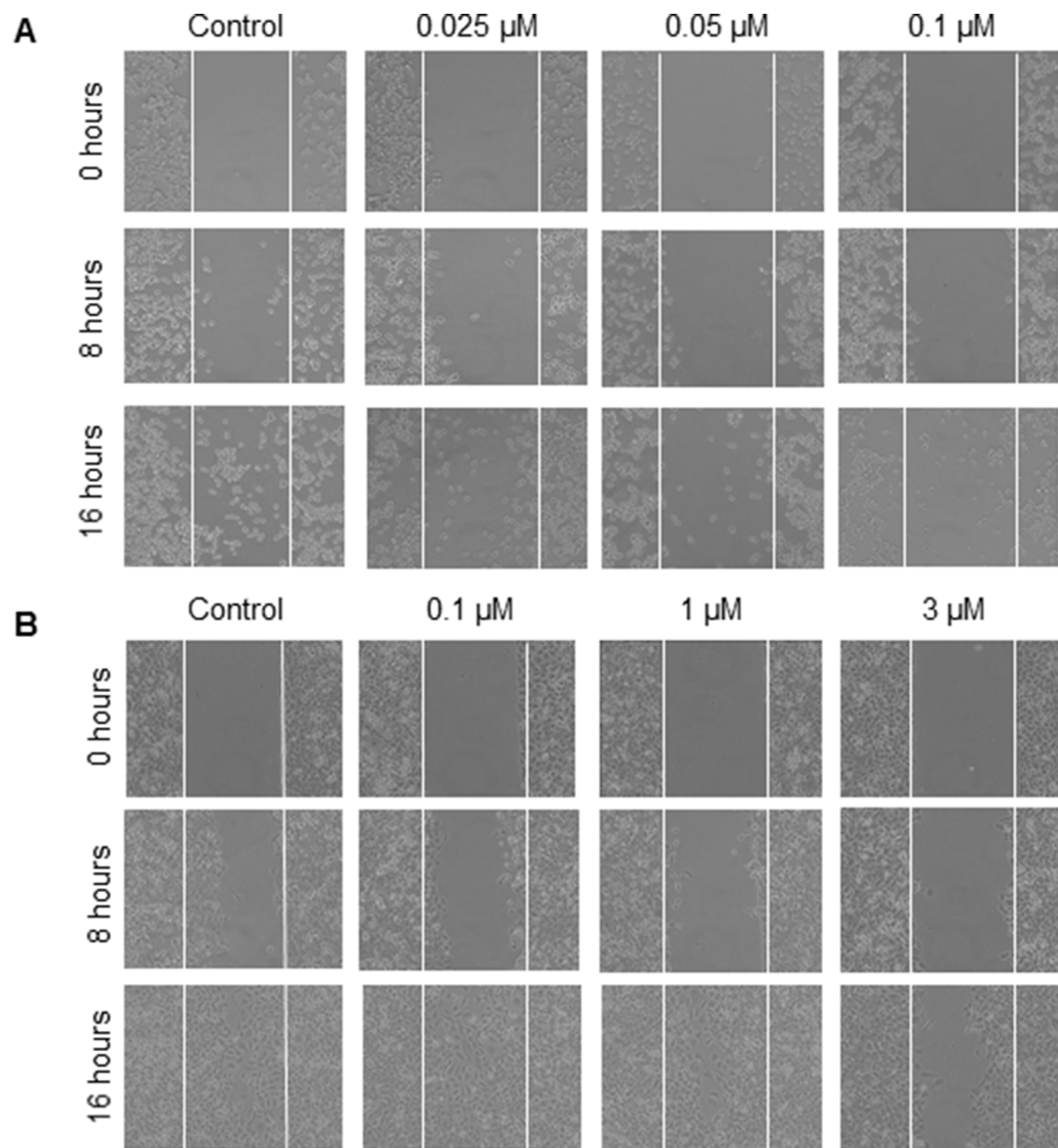
Supplementary Materials



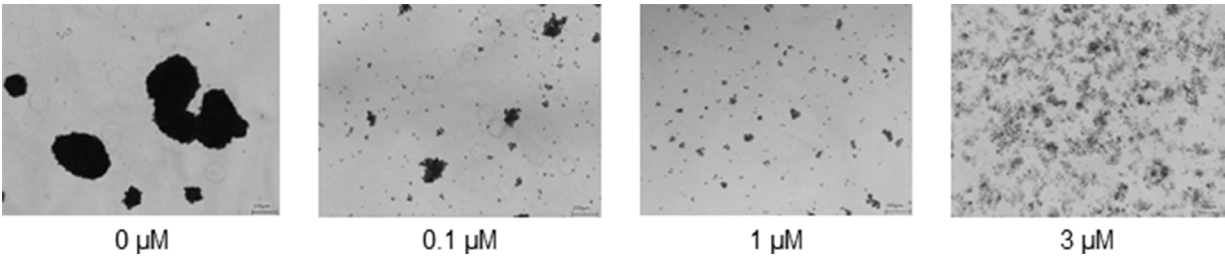
Supplementary Figure 1: Carbenoxolone inhibits LPS-induced HMGB1 secretion: Western blot analysis of Carbenoxolone activation using LPS activation assay. LPS activated Macrophages (M) were incubated with EPI-1 as positive control.



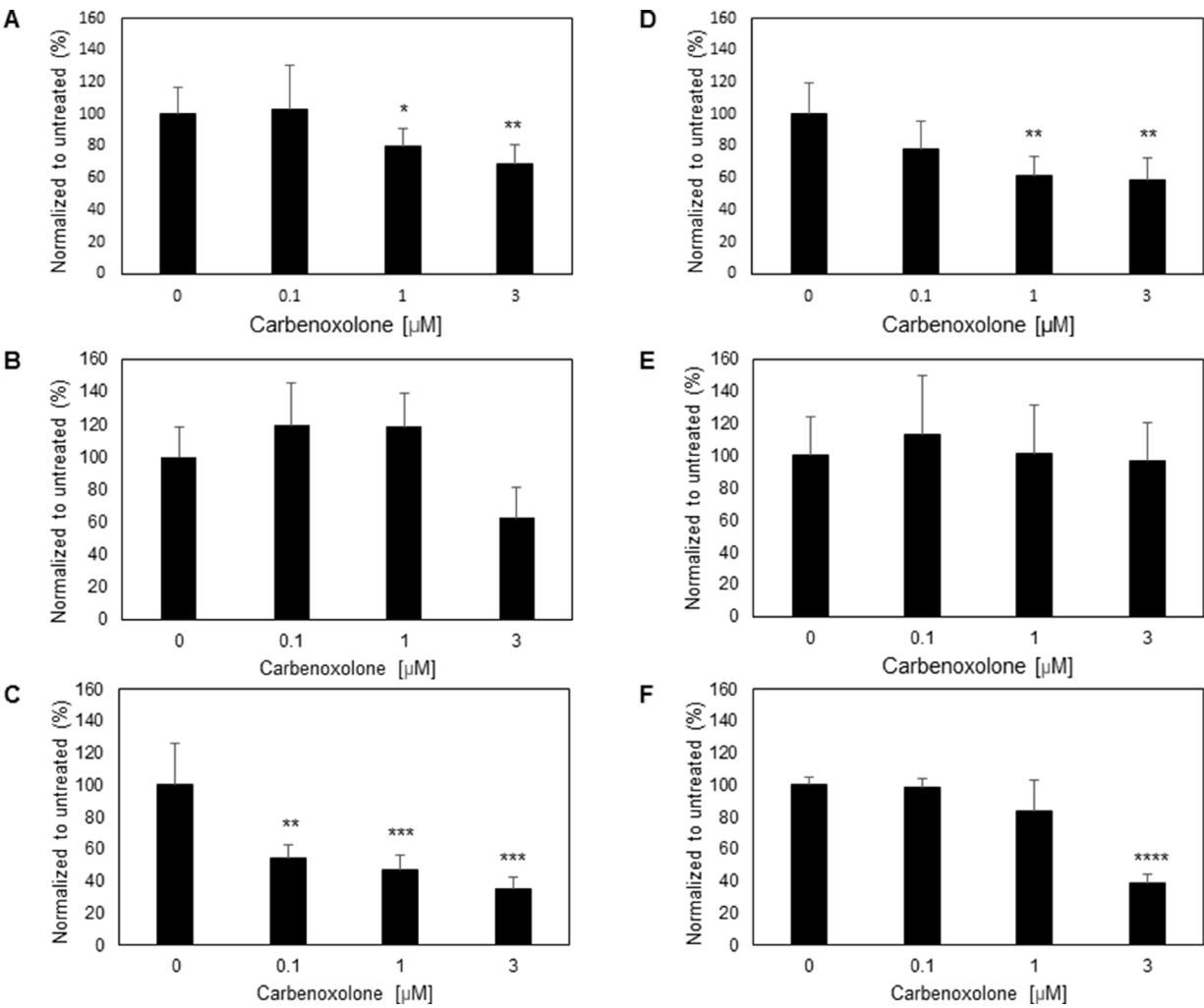
Supplementary Figure 2: Carbenoxolone affects proliferation in different cell lines. Cell proliferation of (A) A-375 (B) LLC and (C) NIH/3T3 cell lines after 72 hours of incubation with Carbenoxolone. $n = 12$. * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$.



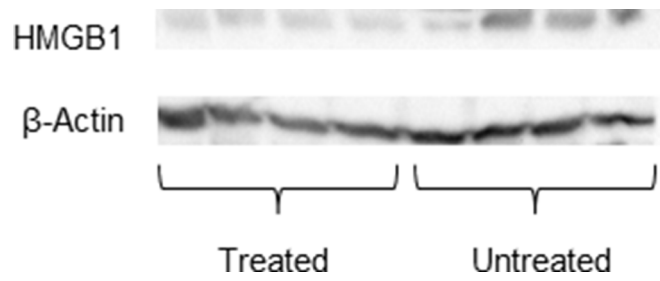
Supplementary Figure 3: Effect of Carbenoxolone on cell migration. Wound healing of (A) LLC and (B) MDA-MB-231 at t0 and post 8 and 16 hours of incubation with Carbenoxolone, with different drug concentration. White thin lines represent the scratch area. $n = 3$.



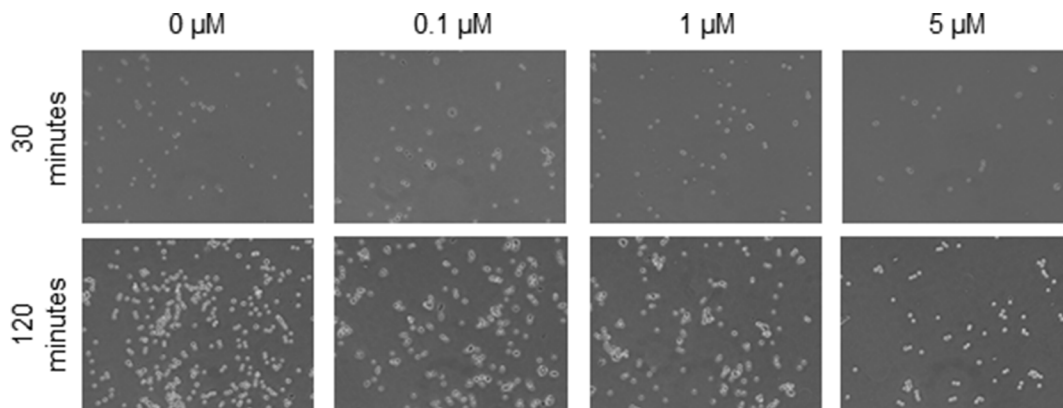
Supplementary Figure 4: Carbenoxolone increases cells' susceptibility to anoikis. Anoikis assay using LLC incubated for 72 hours Carbenoxolone. 100K cells were seeded on p-HEMA coated plates, and cell viability was measured using WST8 with absorbance detected at 450nm using a plate reader. $n = 6$.



Supplementary Figure 5: Collagen is the most affected ECM component resulting Carbenoxolone treatment. Adhesion assay of LLC on plates coated with varying extra cellular matrix components post incubated with Carbenoxolone for 1 hour. Results were normalized compared to the untreated cells of the (A) uncoated plate. Coatings were of (B) fibronectin (C) collagen (D) Laminin (E) Elastin and (F) Gelatin. $n = 6$. * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$.



Supplementary Figure 6: Carbenoxolone lowers level of HMGB1 in tumors of treated mice. Level of HMGB1 in tumors of either treated by Carbenoxolone or untreated mice. $n = 4$.



Supplementary Figure 7: Carbenoxolone has a concentration dependent effect on LLC cells. Adhesion of LLC cells on uncoated culture plates, post 30 and 120 min of incubation with Carbenoxolone. $n = 6$.