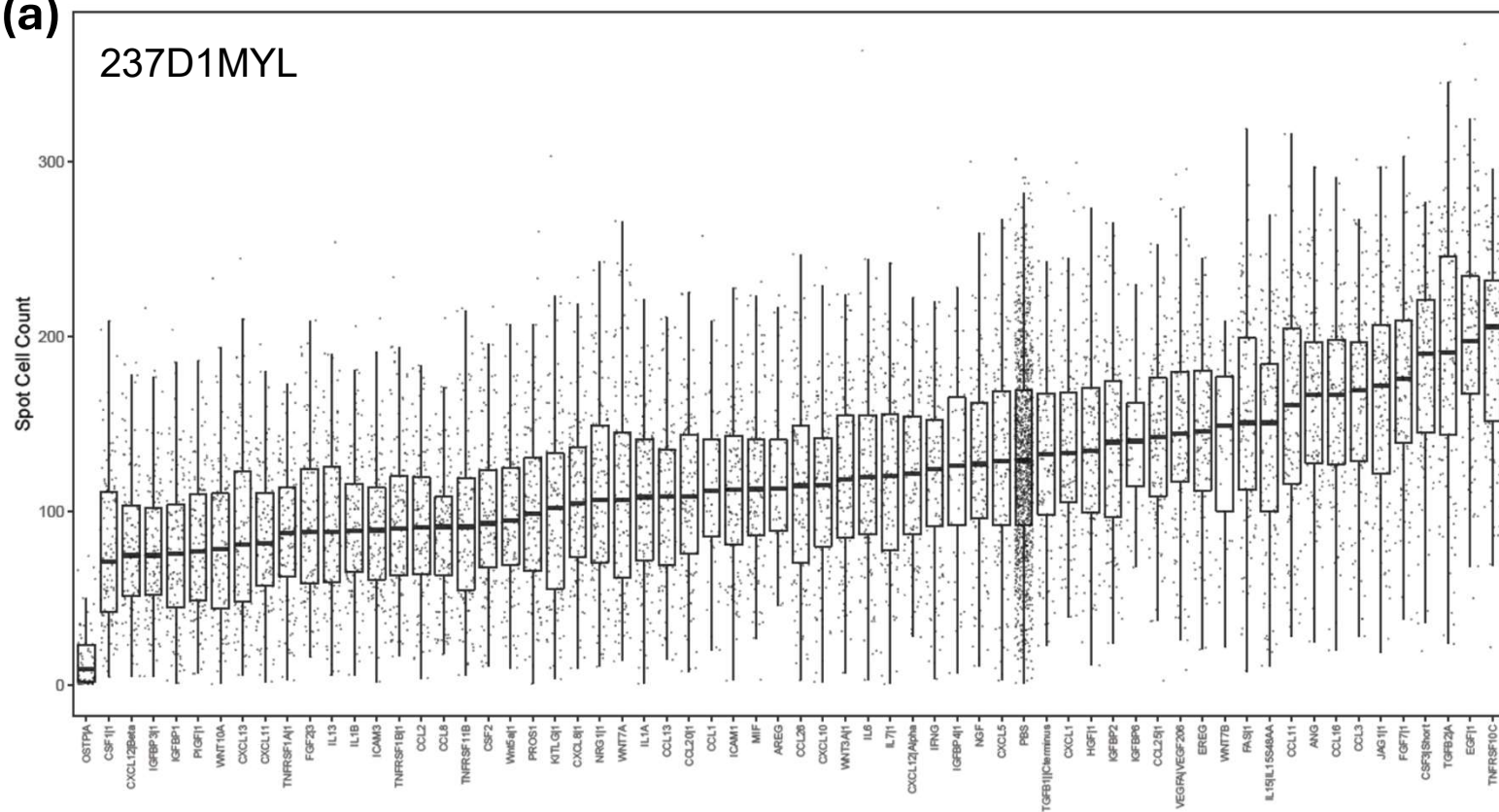
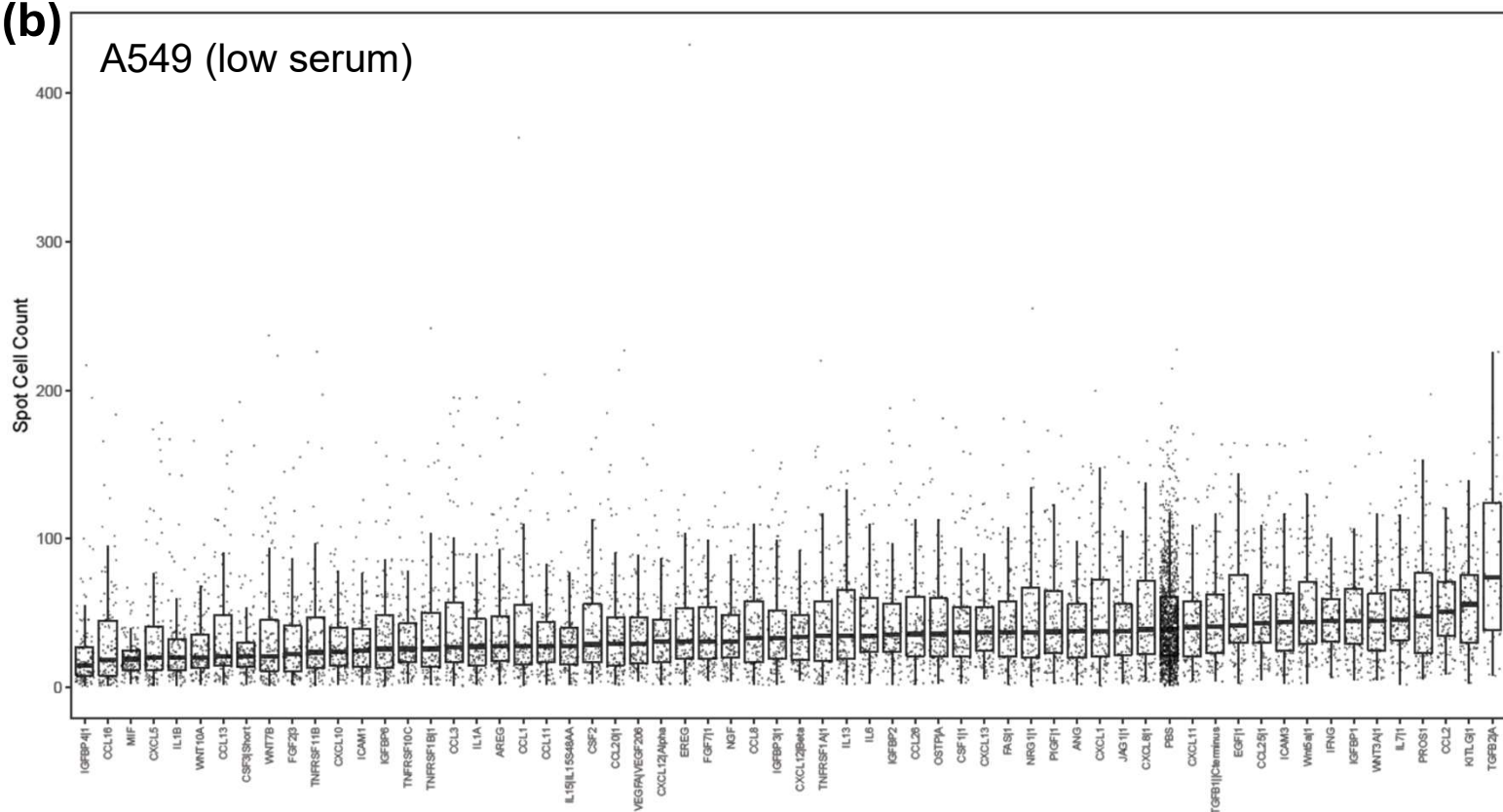
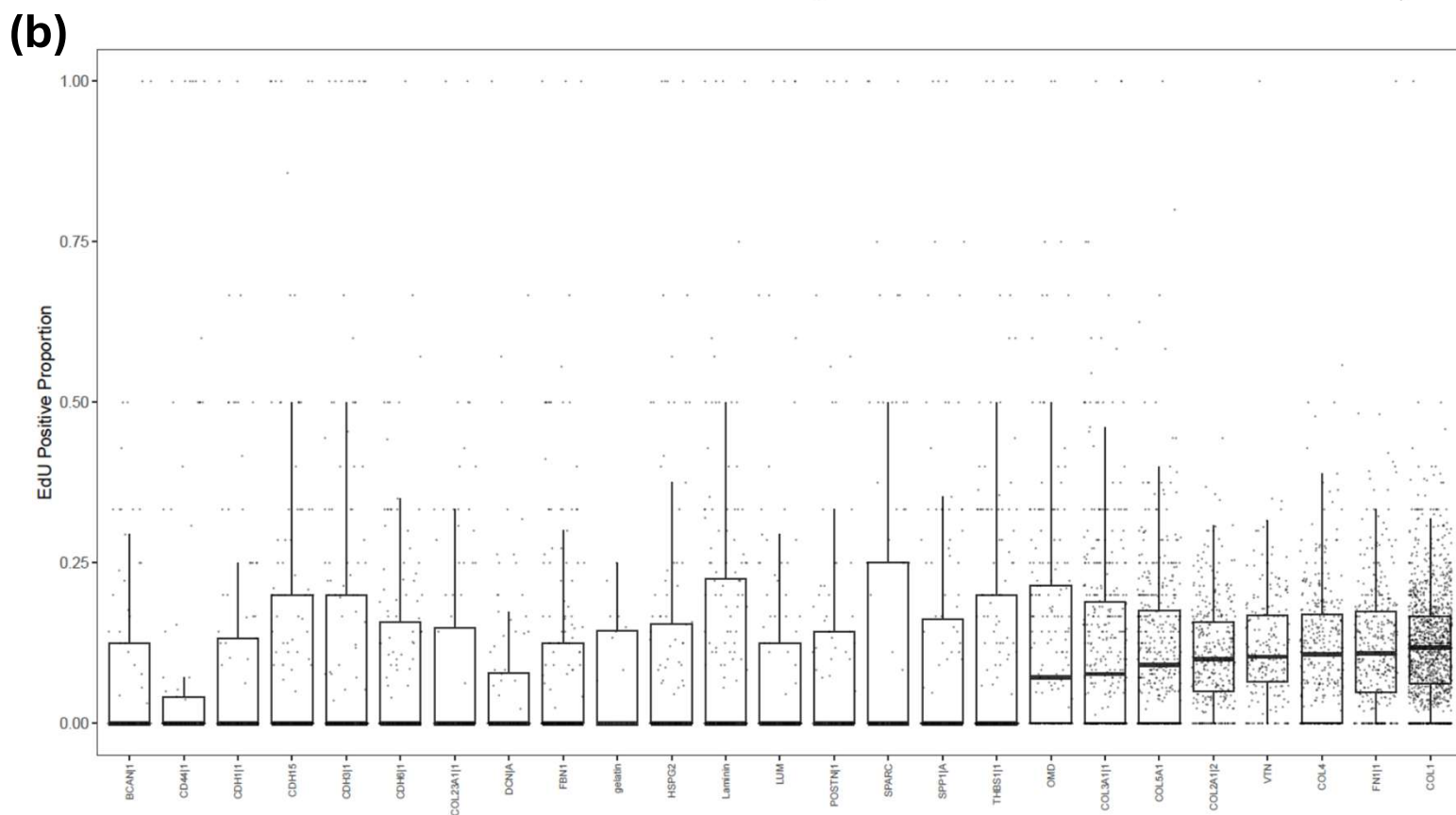
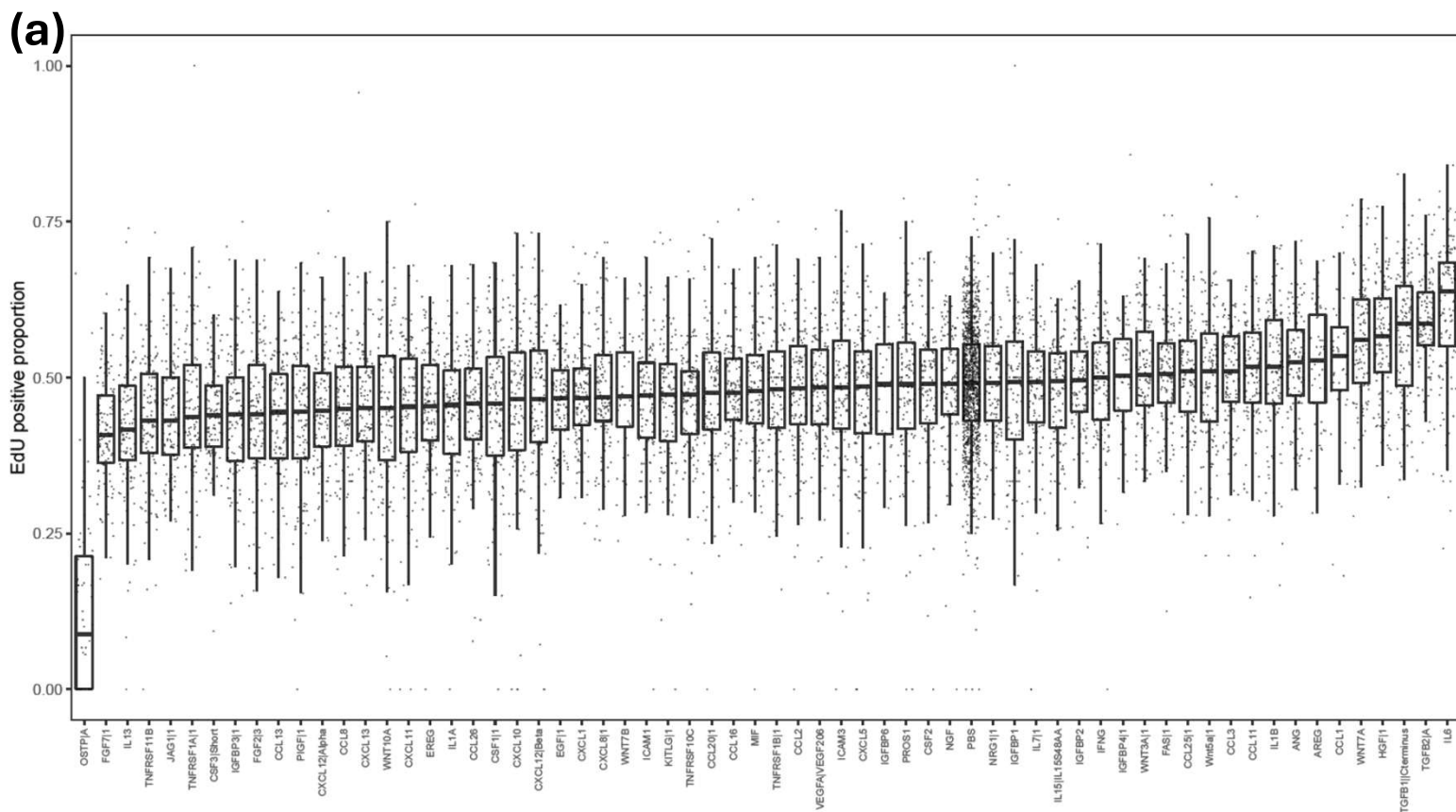
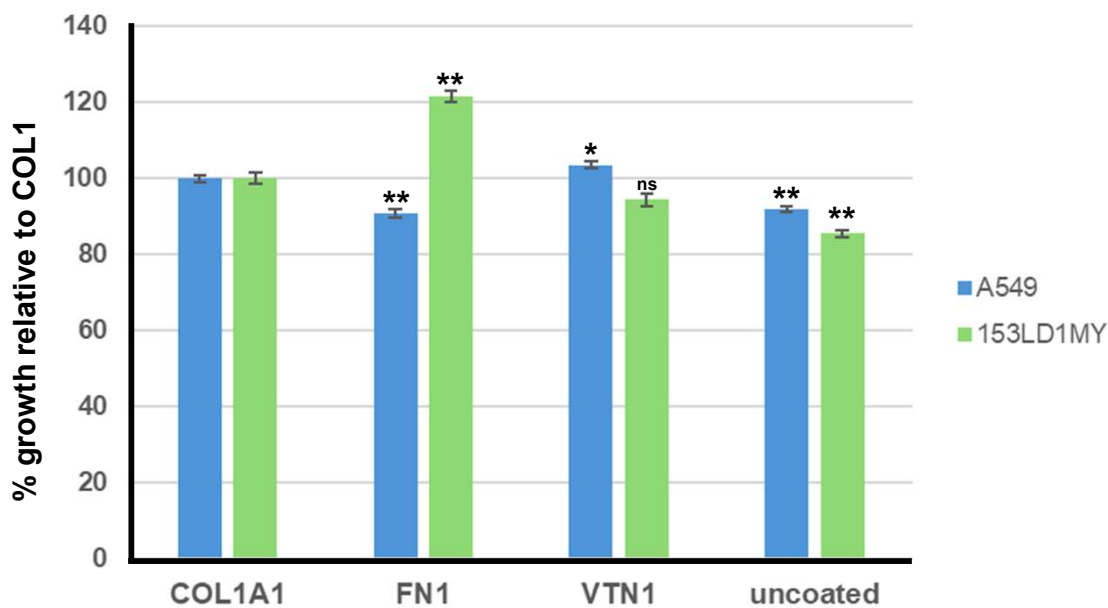


(a)**(b)**

Supplemental Figure 1. Spot cell count for 237D1MYL (a) and A549 (low serum; b) resulting from exposure to different ligands.

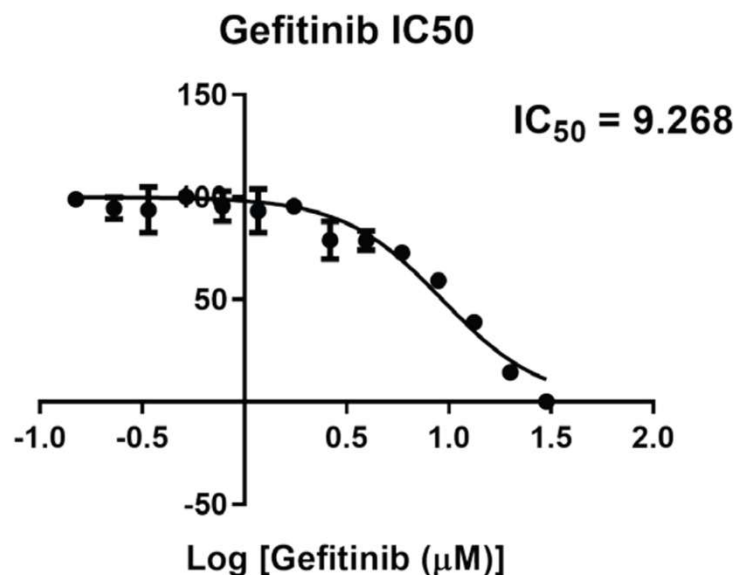


Supplemental Figure 2. EdU positive proportion ordered by ligand for 237D1MYL (a) and ordered by ECM for A549 (b).

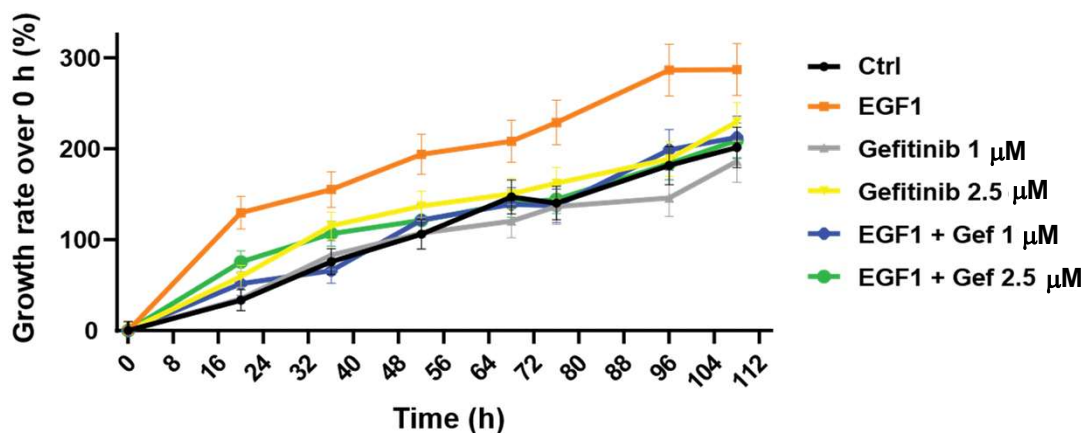


Supplemental Figure 3. Validation of impact of ECM on A549 and 153LD1MY cell growth. % Growth of A549 (blue) and 153LD1MY (green) cells relative to control conditions is dependent on substrate coating. 96 well plates were coated with collagen 1, fibronectin, vitronectin, or left uncoated. Equal numbers of cells were plated in each well and left to grow for 72h, at which time cell number was quantified using CTG readings. Consistent with the results in Fig.1(b) and (c), A549 growth was significantly enhanced by VTN1 and reduced by FN1, while 153LD1MY growth was significantly enhanced by FN1. Bars represent mean of 12 replicate readings; error bars are +/- SEM; * represents significantly different ($p < 0.05$) from control (COL1A1 coated) after Bonferroni corrected; ** represents $p < 0.001$ after Bonferroni correction; ns is not significant.

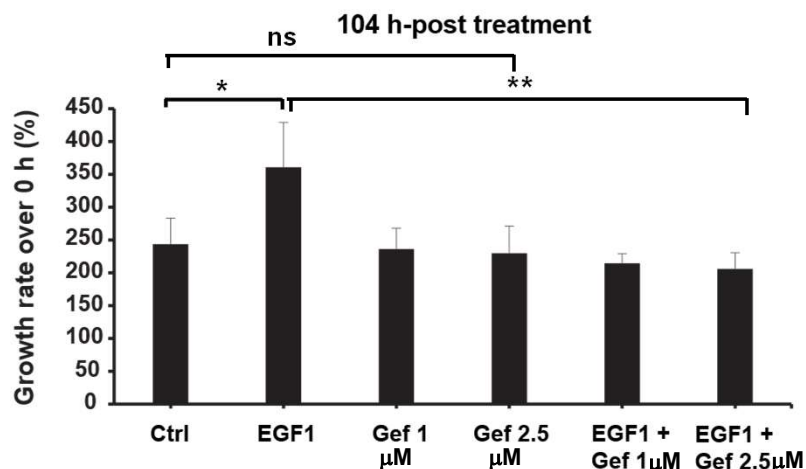
(a)



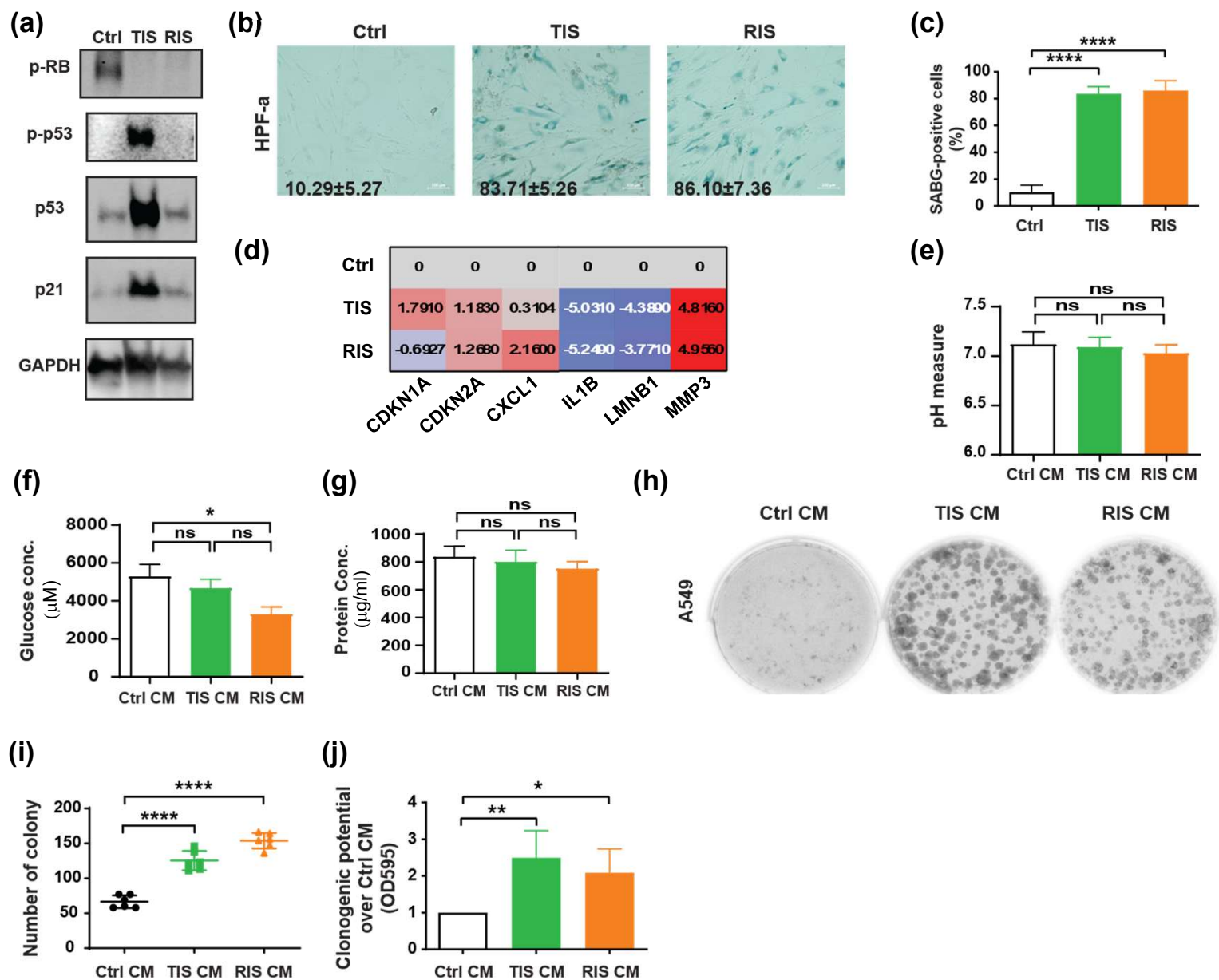
(b)



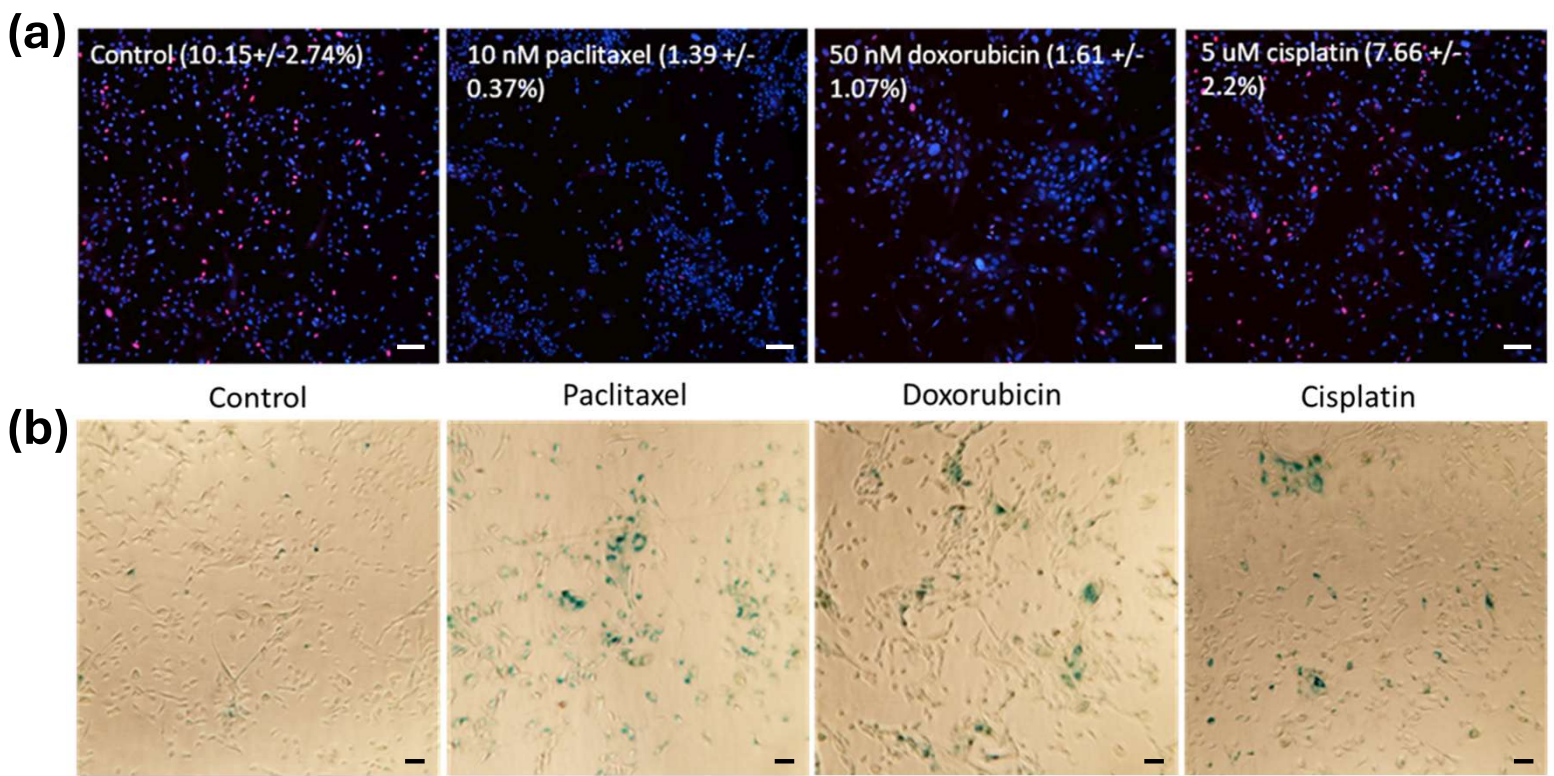
(c)



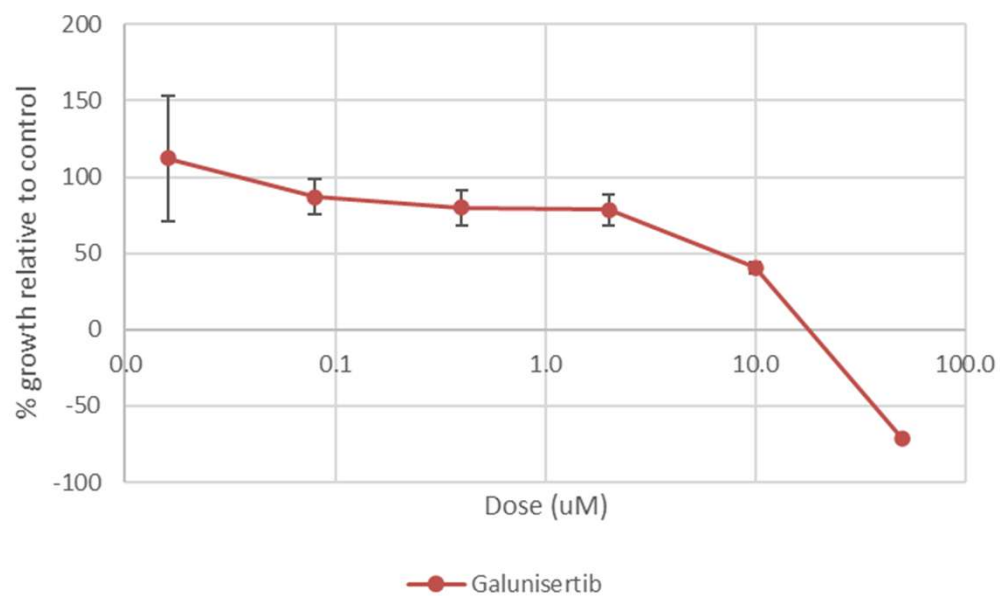
Supplemental Figure 4. Effect of the EGFR inhibitor gefitinib on A549 cell growth. **(A)** A549 cells show limited response to gefitinib over the course of 3 days, with an IC_{50} of 9.268 μ M. **(B)** A549 cells treated with EGF show enhanced growth that is reversed by treatment with gefitinib (1 or 2.5 μ M); in contrast, these doses of gefitinib have no significant effect on A549 in the absence of EGF. Representative data of 3 independent biological repeats are shown as mean $\pm$ SD. **(C)** The growth rate at 104 h-post treatment are shown in bar chart. One-way ANOVA + Tukey HSD test.



Supplemental Figure 5. Characterization of cellular senescence in HPF-a upon treatment with cisplatin or ionising radiation (IR) and corresponding conditioned media (CM). (a) Protein expression of senescence markers in normal HPF-a or senescent HPF-a induced with cisplatin (TIS, therapy-induced senescence) or IR (RIS, radiation-induced senescence). (b-c) Representative images (b) and quantification (c) of HPF-a stained for SA-b-Gal. A549 cells were untreated (Ctrl) or treated with cisplatin or IR for senescence induction. Cells were fixed on Day 10 after senescence induction and subjected to SA-b-Gal staining using Senescence b-Galactosidase Staining Kit (#9860, Cell Signaling). Images were taken using Zeiss Axio Observer 7 microscope and ZEN Blue software (ver 3.1). Scale bar, 100 μm . Data are shown as mean $\pm$ SD from 5 biological replicates. (d) Transcriptional expression of senescence-associated genes detected using quantitative real-time PCR. RNA of A549 cells was extracted on Day 10 after senescence induction and subjected to RT-qPCR. The heatmap are shown as mean fold change in $\log_2$ compared to Ctrl from 3-5 biological replicates. (e-g) Characterization of 72-h CM from Ctrl, TIS, or RIS HPF-a in terms of the pH value (e), glucose concentration (f), and protein levels (g). (h-j) Growth promotion of A549 cells by senescent CM. Colony formation assay was performed to evaluate the impact of senescent CM on the growth of A549. Cells were seeded at a density of 750 cells per well of 6-well plate one day before the treatment. CM treatment was refreshed every 2-3 days throughout the 15-day assay. Representative images (h) and quantification (i-j) of colony formed from 4 biological replicates are shown as mean $\pm$ SD. * $p < 0.05$; ** $p < 0.01$; **** $p < 0.0001$; ns, not significant.



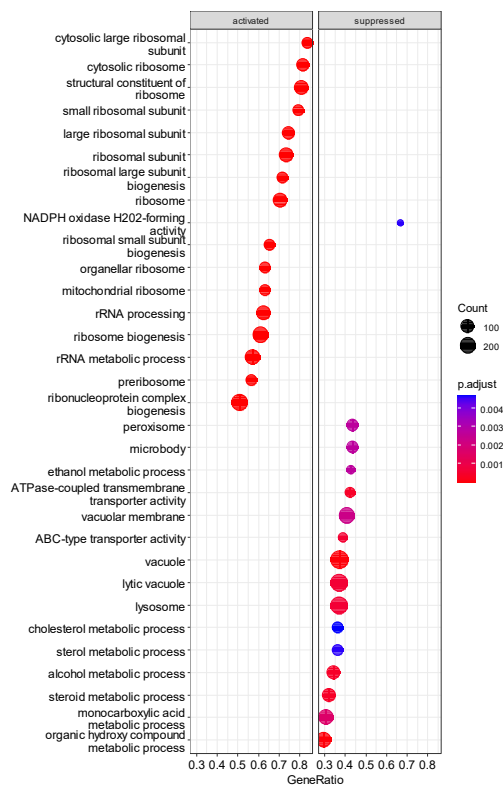
Supplemental Figure 6. Induction of senescence through treatment with chemotherapeutic agents. **A.** Induction of senescence with chemotherapy treatment in the HMEC cell strain 237D1MYL as measured by loss of EdU incorporation or **B.** SABgal staining (**B**). Values in **A** represent percentage of cells positive for EdU incorporation, $\pm$ S.D. from triplicate wells. Scale bar in A is 100 μ m and scale bar in B is 50 μ m.



Supplemental Figure 7. Effect of the TGFBR inhibitor galunisertib on HMEC 237D1MYL cell growth.

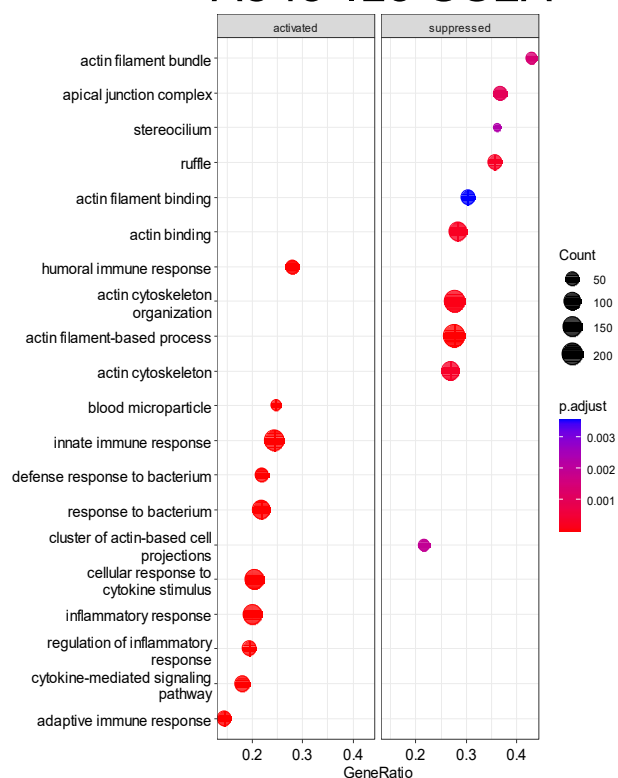
(a)

A549-EGF GSEA



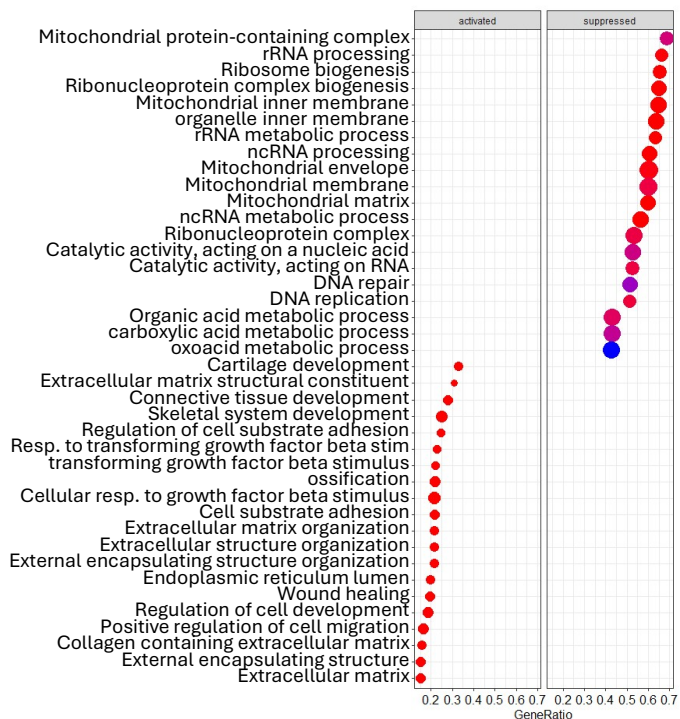
(b)

A549-IL6 GSEA



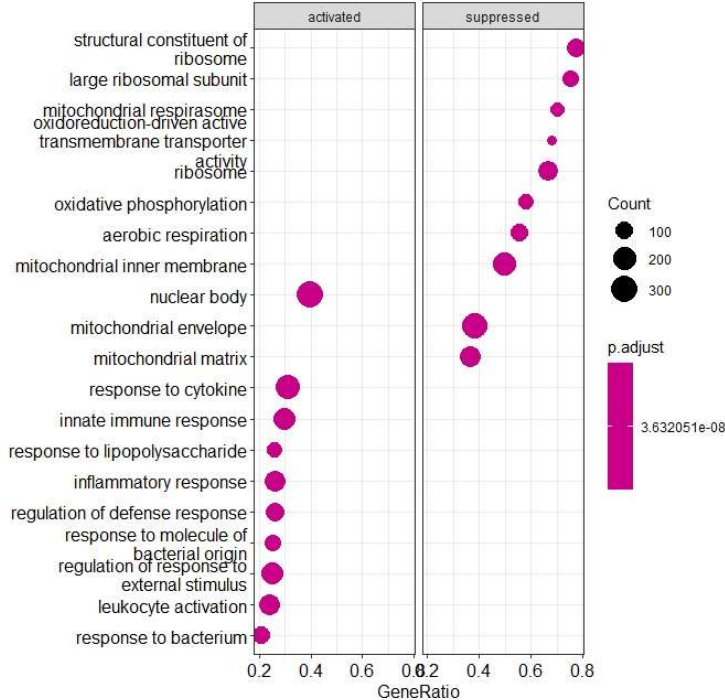
(c)

HMEC-TGFB1 GSEA



(d)

HMEC-IL6 GSEA



Supplemental Figure 8. GO GSEA analysis of responses to treatment in lung cancer and breast HMEC cells. (A) Dotplot of gene sets that were activated or repressed post treatment of A549 cells with EGF1. (B) Dotplot of gene sets that were activated or repressed post treatment of A549 cells with IL6. (C) Dotplot of gene sets that were activated or repressed post treatment with TGFB1 in the HMEC. (D) Dotplot of HMEC gene sets that were activated or repressed post treatment with IL-6 in the HMEC.