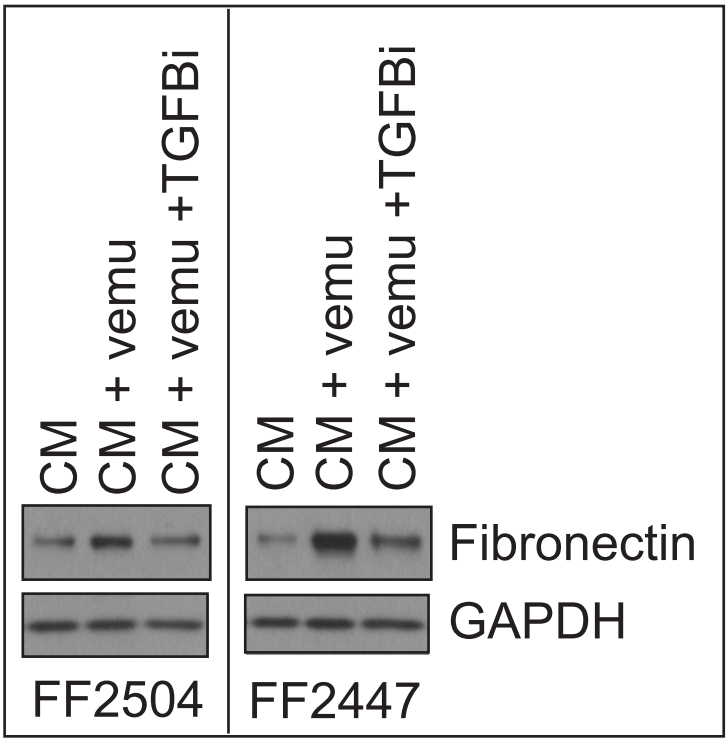
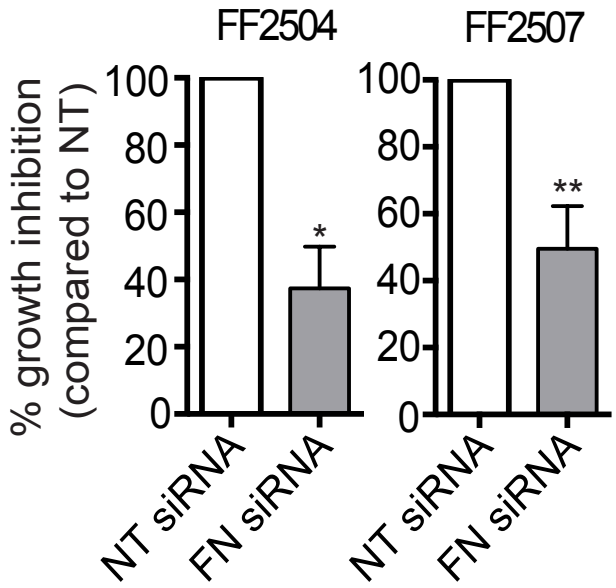
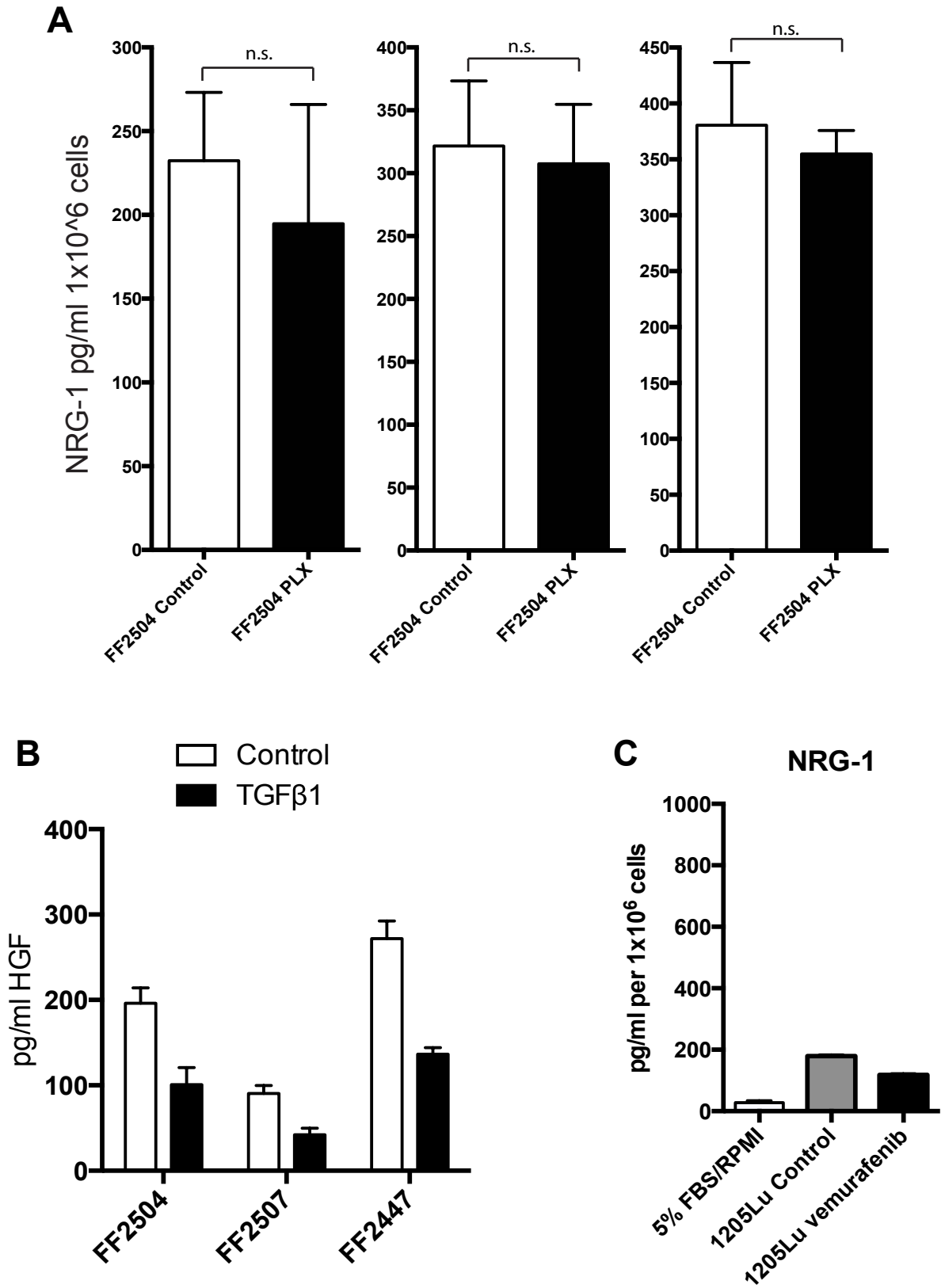


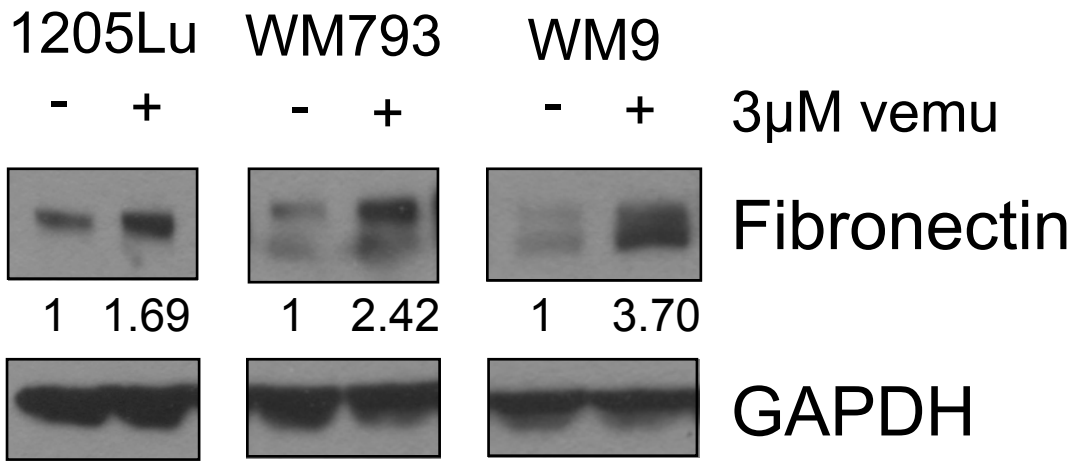
Supplementary Figure 1. Inhibition of TGFβ partially suppressed fibroblast activation. Western blot of FF2504 and FF2447 fibroblast cultures treated with either conditioned media from 1205Lu cells (CM), conditioned media from 1205Lu cells treated with 3μM vemurafenib for 48 hours (CM+vemu), or conditioned media from 1205Lu cells treated with 3μM vemurafenib for 48 hours containing SB505124 (CM+vemu+ TGFβi).



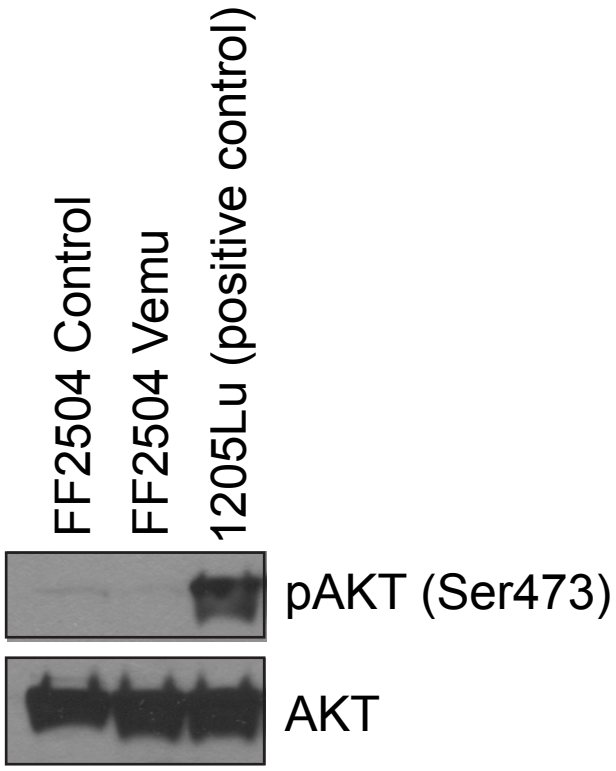
Supplementary Figure 2. FN is required for optimal growth and survival of human primary skin fibroblasts under stress-inducing conditions. FF2507 primary skin fibroblasts were treated with either non-targeting (NT) or FN (FN) siRNA prior to serum starvation (72hours). Cell viability was assessed using Alamar Blue assay, and percentage of growth inhibition was normalized to the NT control.



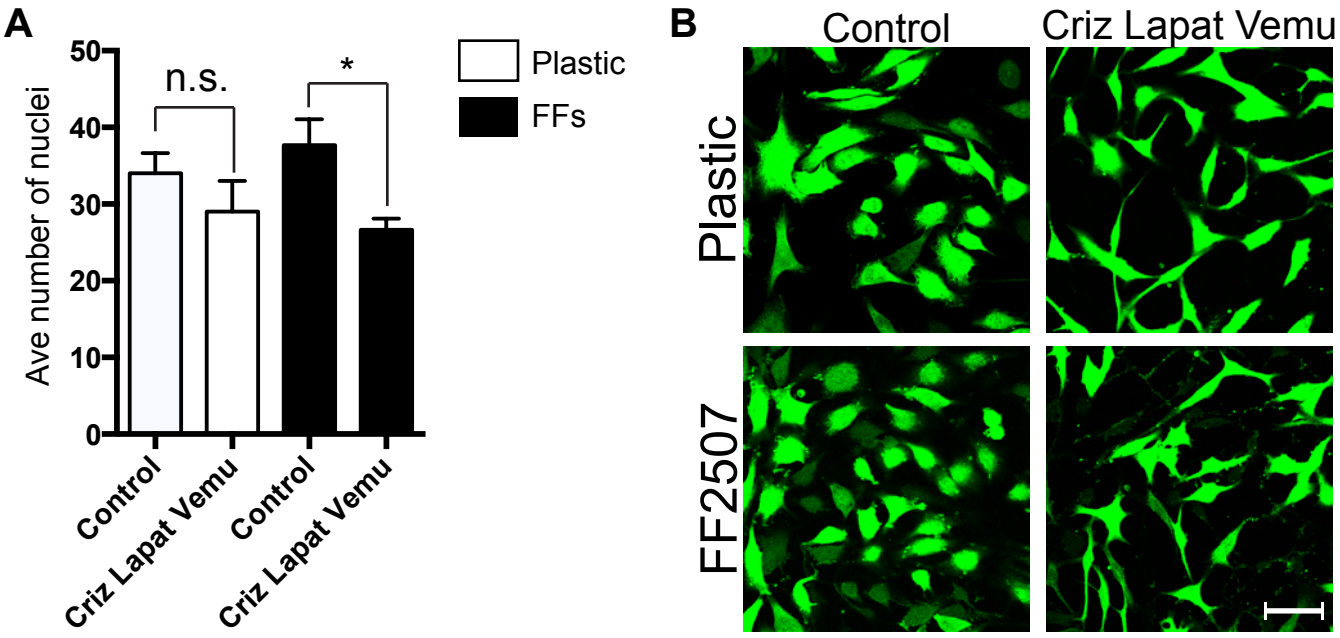
Supplementary Figure 3. Vemurafenib and TGFβ1 do not have the same stimulatory effects on fibroblasts. A. Vemurafenib does not induce NRG release from fibroblasts. ELISA data showing NRG release from 3 human skin fibroblast cell lines, following treatment with 3μM vemurafenib for 72 hours. B. TGFβ1 does not induce HGF release from fibroblasts. ELISA data showing HGF release from 3 human skin fibroblast cell lines, following treatment with 3μM vemurafenib for 72 hours. **C.** Melanoma cells do not secrete NRG-1 in response to vemurafenib. ELISA data showing NRG release from 1205Lu melanoma cell line, following treatment with 3μM vemurafenib for 72 hours.



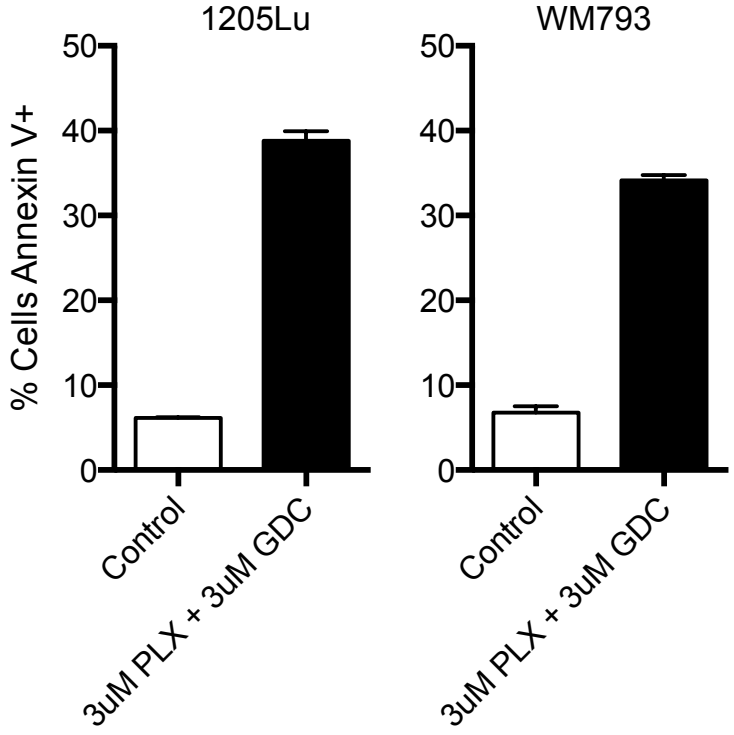
Supplementary Figure 4. FN induction in melanoma cells in response to vemurafenib. Western blot data showing FN upregulation from 3 BRAFV600E human melamoma cell lines, following treatment with 3μM vemurafenib for 48 hours.



Supplementary Figure 5. Vemurafenib does not induce pAKT in primary skin fibroblasts. Western blot data showing pAKT and AKT levels in FF2504 primary skin fibroblasts following treatment with 3μM vemurafenib for 24 hours. 1205Lu basal lysate is included as a positive control.



Supplementary Figure 6. Melanoma cell proliferation with triple inhibition of BRAF, MET and HER2. A. Melanoma cells treated with vehicle control or the combination of 3 μM vemurafenib (BRAFi), 200 nM crizotinib (METi), and 1 μM lapatinib (HER2i). Cells were plated either on cell culture plastic or a confluent monolayer of FF2507 fibroblasts and treated for 24 hours prior to analysis of cell counts. The average number of GFP+ nuclei in each treatment using Definiens® Developer v2.0 software suite. **B.** Representative images of GFP+ melanoma cells from A. Scale bar = 50 μm.



Supplementary Figure 7. The effects of BRAFi+PI3Ki combination on plastic. Melanoma cells were plated on cell culture plastic overnight and treated with vehicle control or the combination of 3 μM vemurafenib (BRAFi) and 3 μM GDC-0941 (PI3Ki) for 72 hours before being stained for annexin-V and analyzed by flow cytometry.