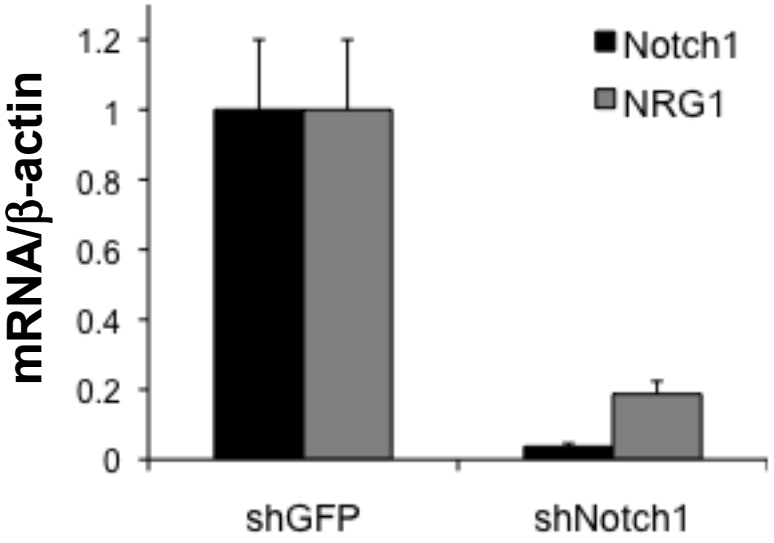
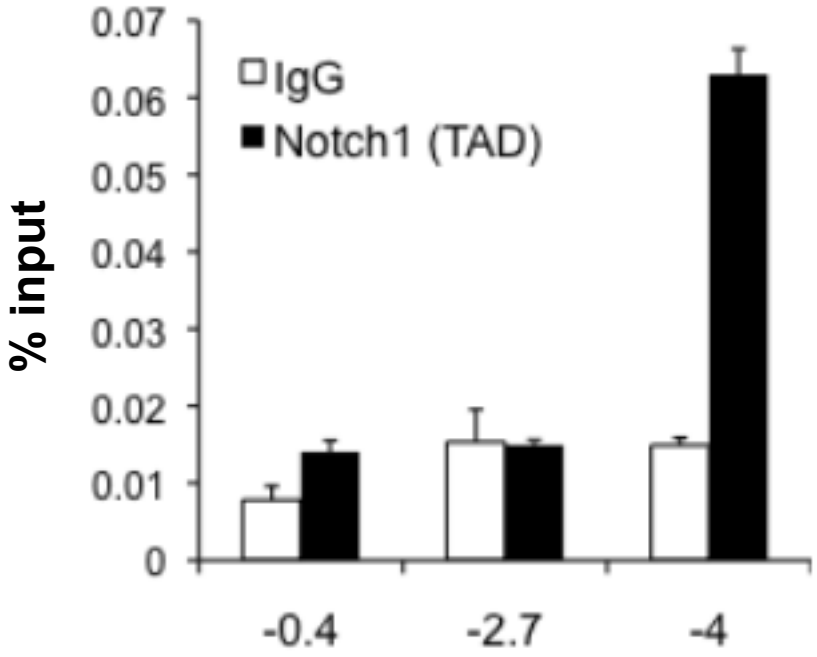


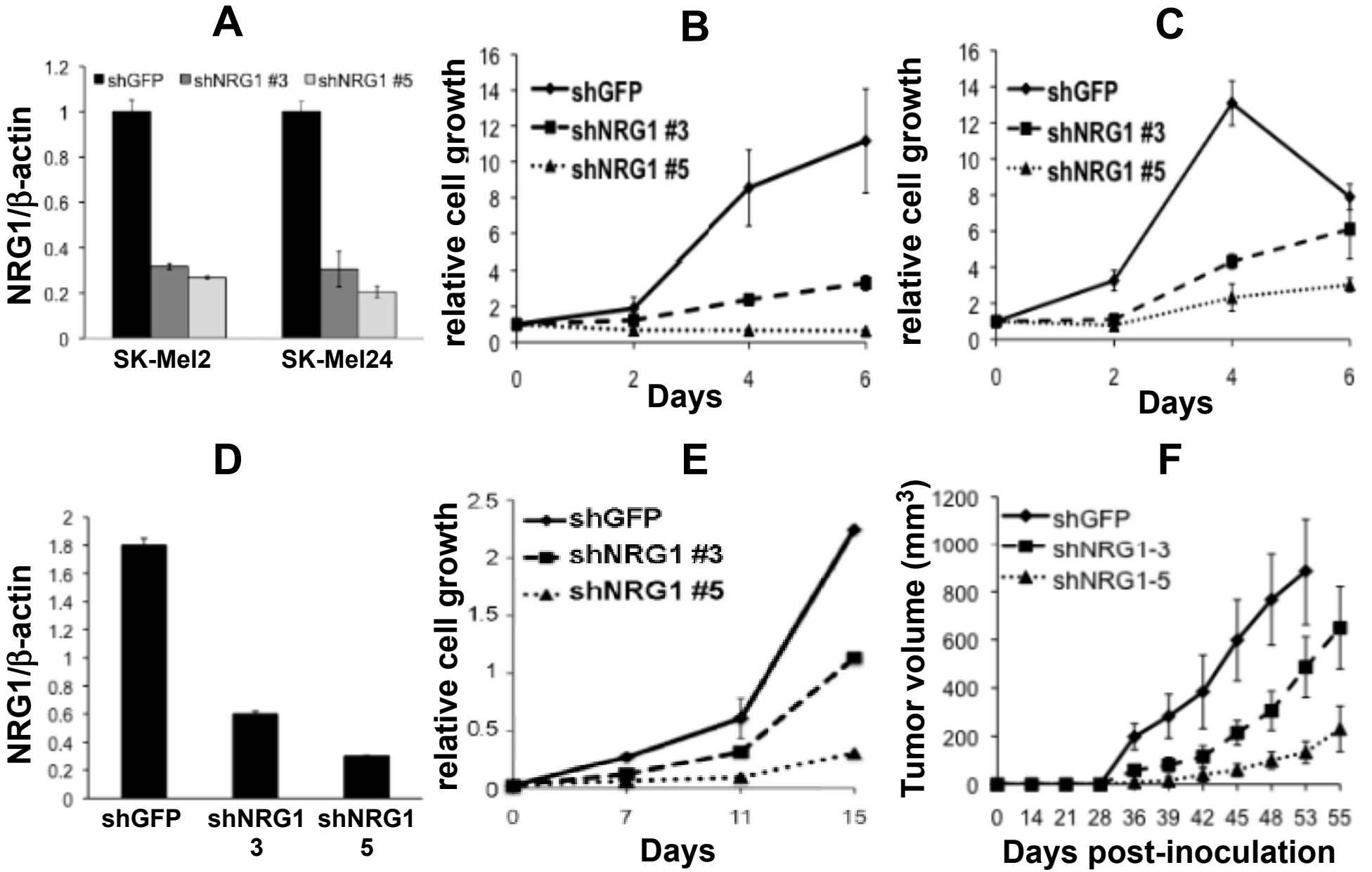
Supplementary figure 1. NRG1 expression is reduced by Notch1 inhibition: K457 melanoma cells expressing a specific shRNA against Notch1 (shN1-2) show a significant reduction in both Notch1 and NRG1 mRNA.

Zhang et al, suppl fig. 1



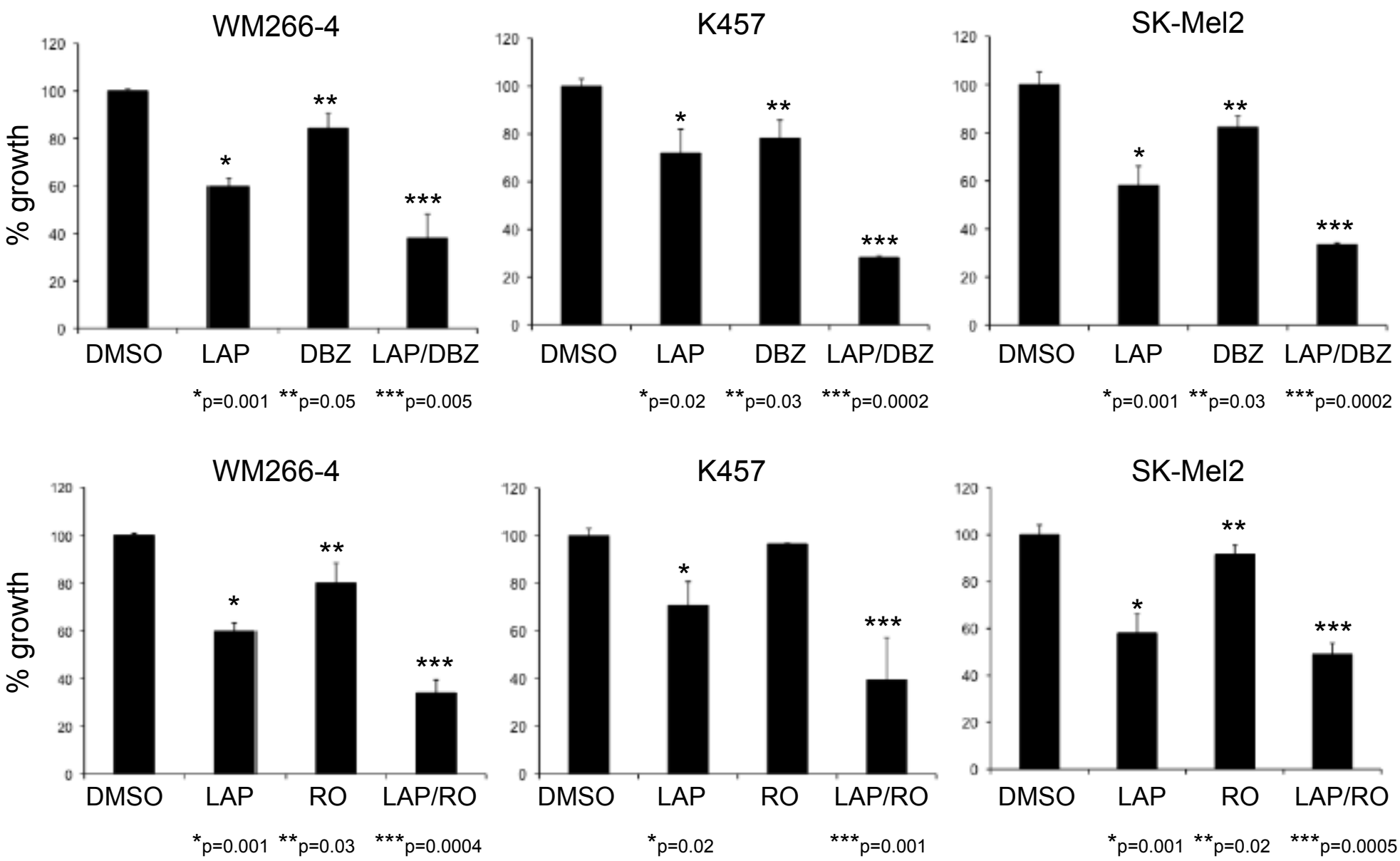
Supplementary figure 2. Notch1 occupancy of the three putative CSL-Notch1 binding sequences in the NRG1 promoter region: ChIP analysis showing association of Notch1 to the CSL hexamer at position -3805 Kb. The sites at -0.403 Kb and -2.7 Kb show absence of binding. The ChIP assay was performed on K457 cells.

Zhang et al, suppl. fig. 2



Supplementary figure 3. NRG1 knock down inhibits melanoma growth. A) qRT-PCR on SKMel2 and SKMel24 cells expressing shGFP (control) or shNRG1-3 and shNRG1-5, showing 70% and 75% or 70% and 80% inhibition of NRG1 mRNA in SKMel2 and SKMel24, respectively, with either shNRG1-3 or -5. Growth curves for SKMel2 **(B)** and SKMel24 **(C)** showing significant inhibition when NRG1 expression is knock down. **D)** qRT-PCR on K457 cells. The growth of K457cells is inhibited both in vitro **(E)** and in vivo **(F)** by depletion of NRG1 in a manner that correlates with the level of inhibition of NRG1 by the different shNRG1 sequences employed. differences in in vitro growth are statistically significant ($P<0.01$, Student's T test) as calculated by comparing the last time point, except for SK-Mel24 in which the comparison was done at the 4 day time point due to overgrowth of the control (shGFP) at day 6. Tumor growth differences are statistically significant (shGFP vs shNRG1-3, $P=0.01$; shGFP vs shNRG1-5, $P=0.01$; shNRG1-3 vs shNRG1-5, $P=0.02$, Student's T test).

Zhang et al, suppl. fig. 3



Supplementary figure 4. Melanoma growth inhibition by the concomitant treatment with lapatinib and a GSI inhibitor. WM266-4, K457 and SK-Mel2 human metastatic melanoma cells were treated for four days in culture with the EGFR/ERBB2 inhibitor Lapatinib (20 μM), and the GSIs dibenzazepine (DBZ at 10 μM) or RO4929097 (RO at 10 μM), either alone or in combination. All treatments significantly reduced cell growth except for RO4929097 on K457 cells. The highest level of inhibition was observed with lapatinib in combination with a GSI. Growth was evaluated by the crystal violet staining. Significance was calculated by the Student's T test.

Zhang et al. suppl. fig. 4