

Figure S1. Hyperplasia was observed in both the KrasG12D;CD44^{+/-} and KrasG12D;CD44^{-/-} mice at similar levels in 6-week after Ad-Cre infection of lungs. Percentage of area of hyperplasia of total lung is shown. Error bar indicates s.e.m, n = 4.

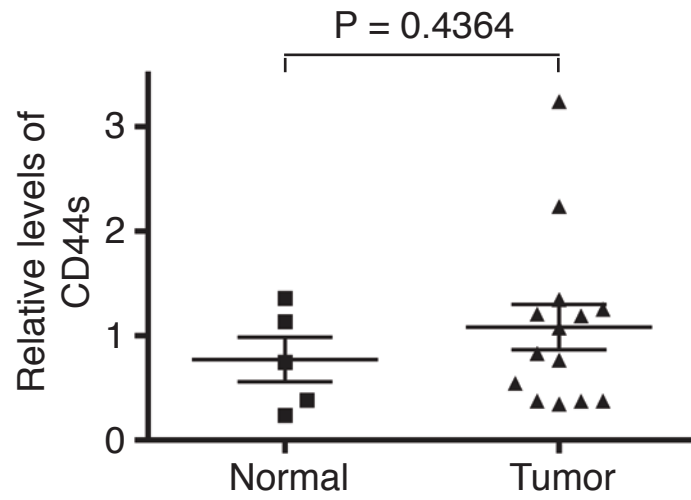


Figure S2. Expression of CD44s in Kras-dependent lung adenocarcinoma tumors in mice. P value was calculated using a two-tailed Student's t test.

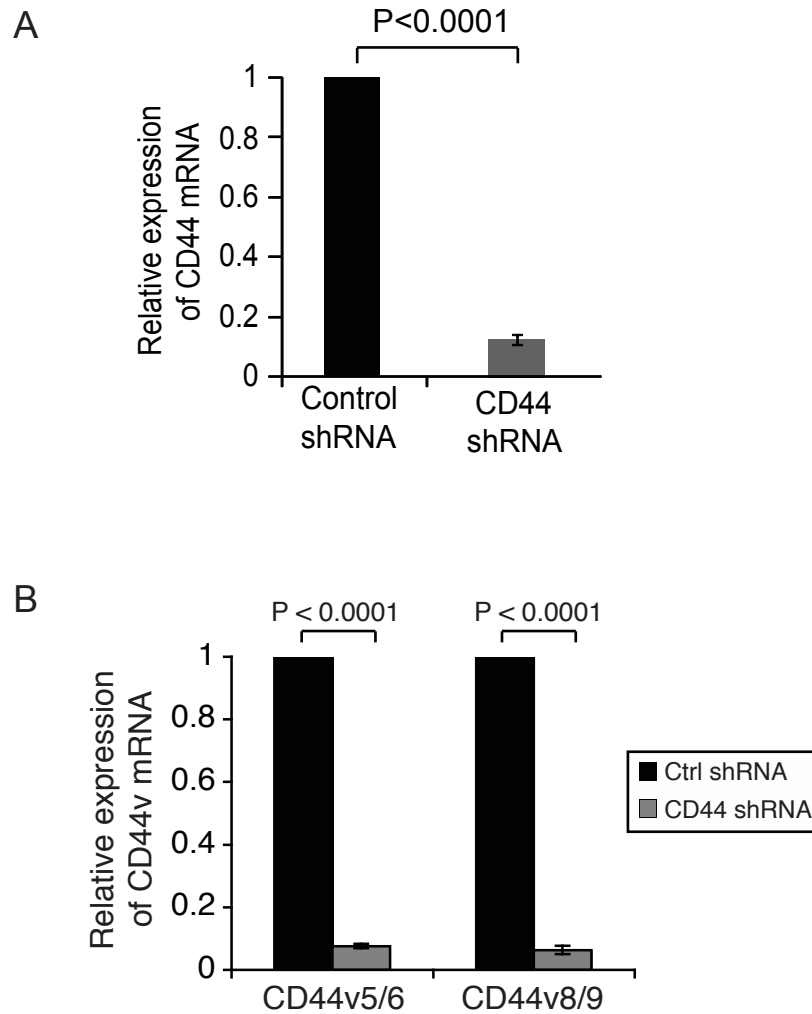


Figure S3. CD44 shRNA efficiently knocks down CD44 in the H358 human lung adenocarcinoma cell line. Results of qRT-PCR analysis of total CD44 (A) and CD44 variants that contain v5/6 and v8/9 variable exons (B) were shown. Primer sequences used were: total CD44 forward: 5'-GATG GAGAAAGCTCTGAGCATC-3', reverse: 5'-TTGCTGCACAGATGGAGTTG-3'; CD44v5/6 forward: 5'-GTAGACAGAAATGGCACCAC-3', reverse 5'-CAGCTGTCCCTGTTGTTCGAA-3'; CD44 v8/v9 forward: 5'-TCC AGT CAT AGT ACA ACG CT-3', reverse: 5'-TGCTTGATGTCAG AGTAGAAGT-3'.

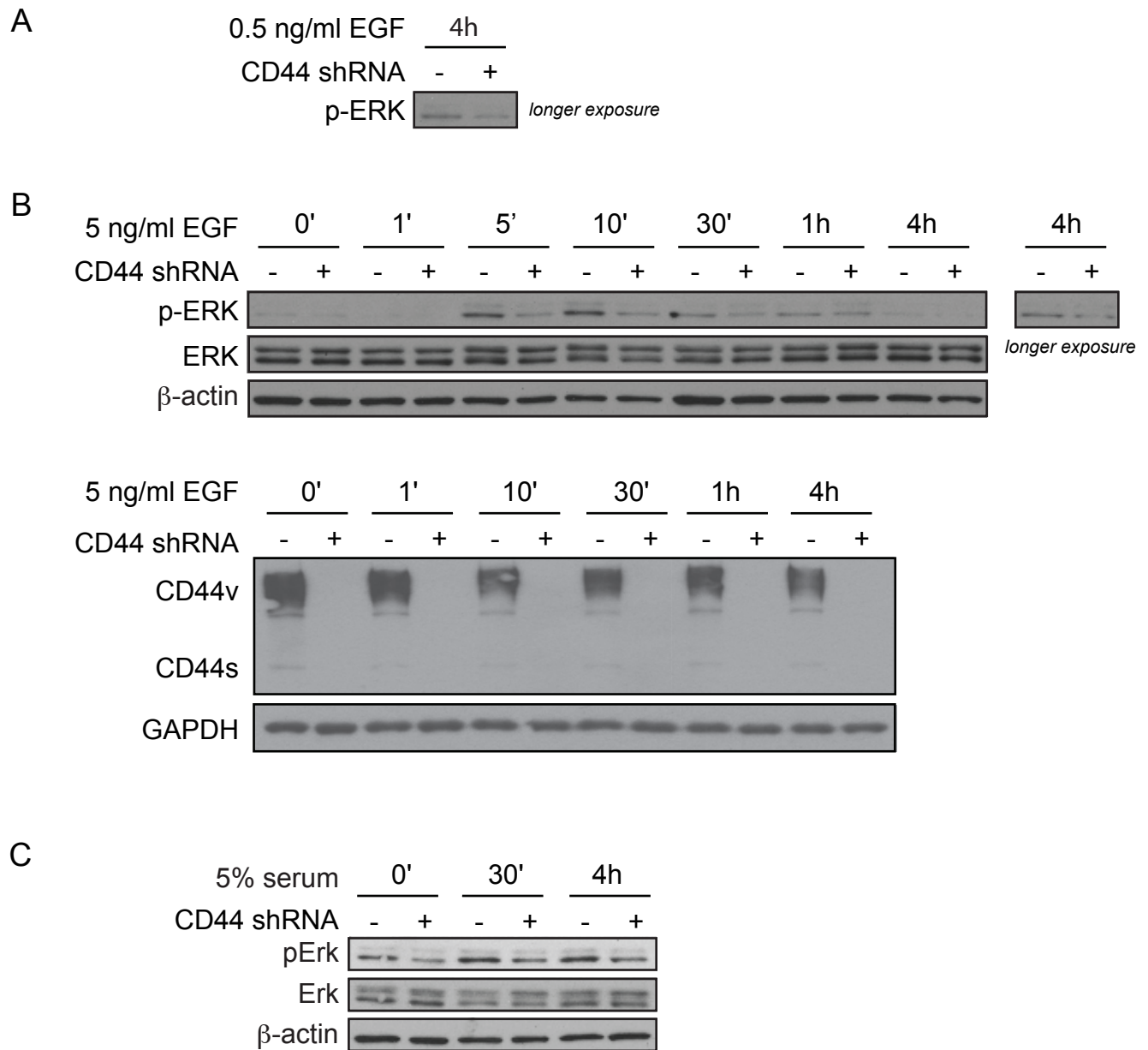


Figure S4. CD44 knockdown impairs Erk activation in H358 cells. A. A longer exposure image of p-Erk levels was shown in control and CD44 knockdown cells that were stimulated with 0.5 ng/ml EGF for 4 h. B. Immunoblot analysis of p-Erk activity (top panel) and CD44 (bottom panel) were shown in control and CD44 shRNA-expressing cells. Cells were serum starved and then stimulated with EGF (5 ng/ml) at different time intervals as indicated. C. Immunoblot analysis of p-Erk activity in control and CD44 shRNA-expressing cells that were stimulated with 5% serum. A longer exposure of p-Erk image is shown.

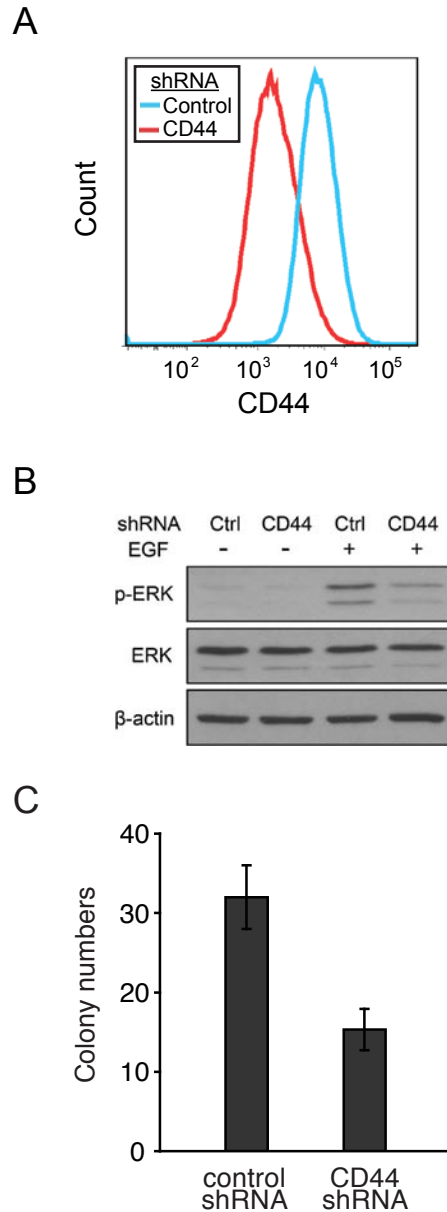


Figure S5. Knockdown of CD44 inhibits Erk activation and colony formation in LKR13 cells. A. FACS analysis showing that CD44 level is downregulated in CD44 shRNA-expressing cells. The mouse CD44-targeted shRNA sequence ACAGGCTTTCAACAGTACCTTA and a nonspecific control shRNA sequence ATCTCGCTTGGGCGAGAGTAAG were cloned into the LMP Retroviral vector (Open Biosystems). B. Immunoblot of phospho-Erk in control and CD44 shRNA-expressing cells. Cells were stimulated with EGF (10 ng/ml) for 2 h after 24 h of serum starvation. β -actin serves as a loading control. C. Analysis of colony assay in soft agar. 1×10^4 LKR-13 cells expressing control or CD44 shRNAs were grown in soft agar in 6 cm plates and numbers of colonies were plotted. s.d. n = 3.