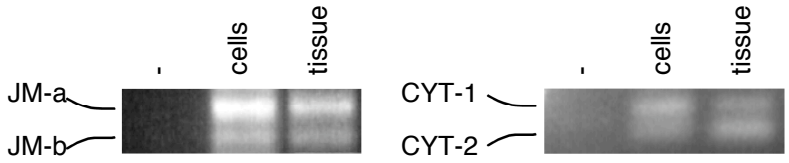
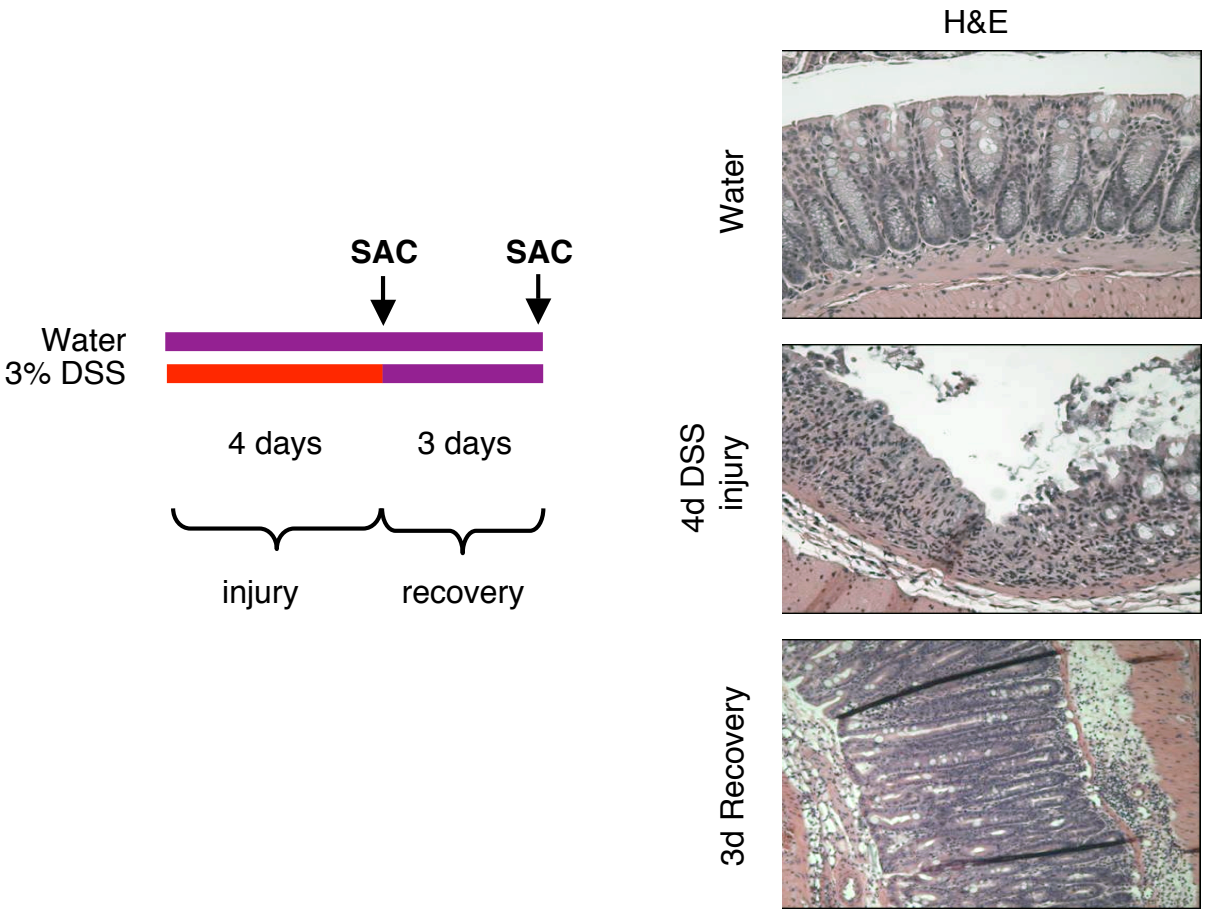
(A)



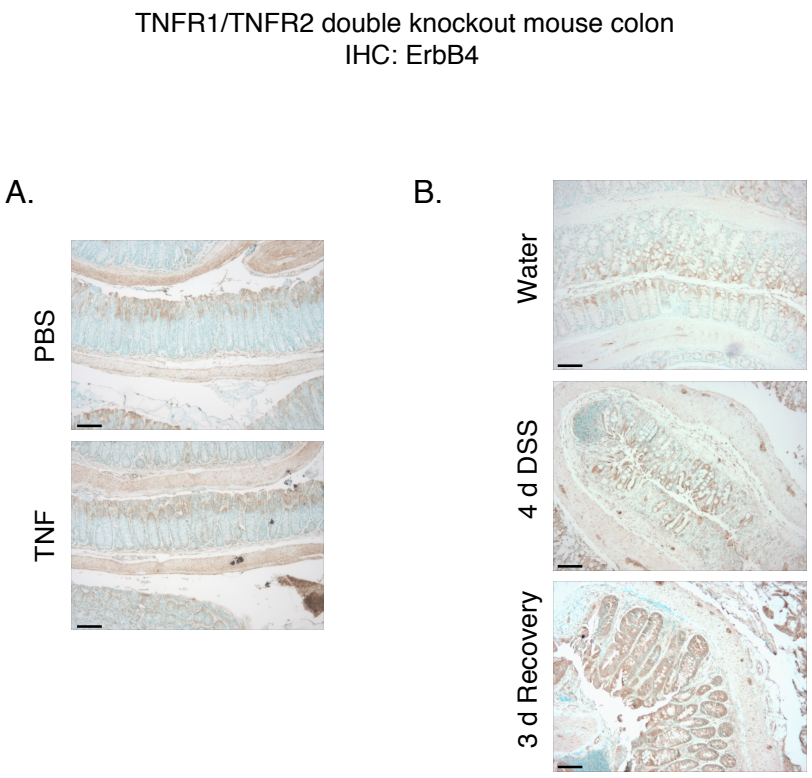
(B)

	JM-a/JM-b		CYT-1/CYT-2	
	Ratio	P < 0.05?	Ratio	P < 0.05?
YAMC Cells	1075+/-122	Y	0.764+/-0.12	N
Mouse colon mucosal lysates	4488+/-951	Y	0.729+/-0.05	N

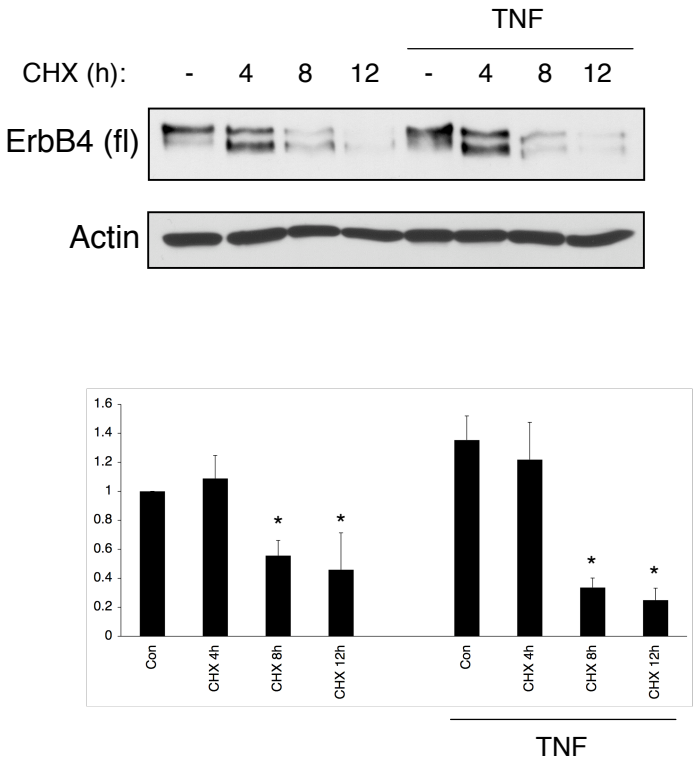
Supplementary figure 1. Expression of ErbB4 isoforms in young adult mouse colon epithelial cells and mouse colon. (A) Total RNA prepared from cultured cells or 4-week old mouse colon was subjected to standard endpoint (non-quantitative) rtPCR using ErbB4 primers which detect either both the JM-a and JM-b isoforms or both the Cyt-1 and CYT-2 isoforms. -, no RT control with cultured cells (identical results with tissue). (B) Quantitative real-time PCR was performed using primer sets specific to each isoform to establish JM-a/b and CYT-1/2 expression ratios.



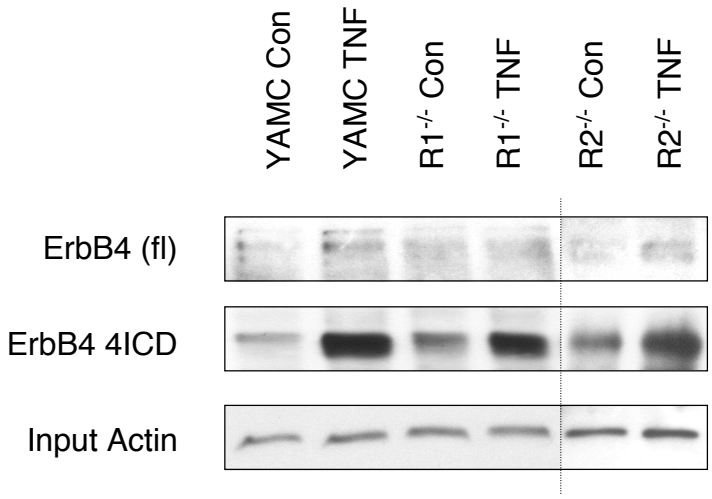
Supplementary figure 2. Schematic and histology of acute DSS colitis. Mice were given 3% DSS (w/v) in drinking water for 4d as shown in diagram to induce colonic ulcers and wound healing responses. H&E shows ulcerated region (middle panel) and hyperproliferative regrowth phase (bottom panel). During injury/ulceration phase, significant regions of spared epithelium are also present (see Fig. 2).



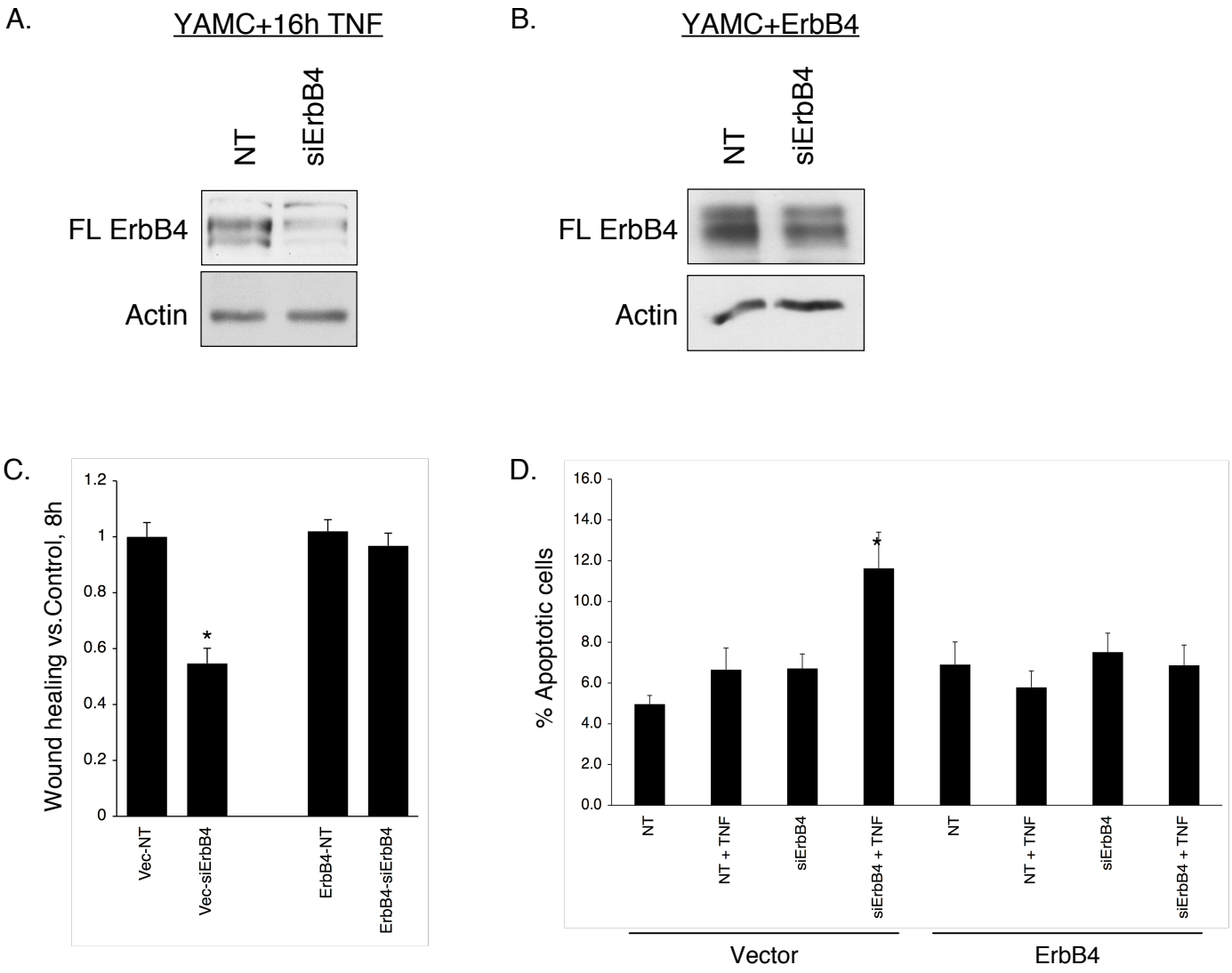
Supplementary figure 3. TNF signaling is partially required for ErbB4 induction during murine DSS colitis and recovery. (A) TNFR1/TNFR2 double-knockout mice were injected with TNF (10^4 U TNF, 24 h). Fixed colon tissue was immunostained for ErbB4 expression and localization. (B) Mice were given DSS (3%) for 4d, or 4d followed by 3d recovery. Bars, 100 μm.



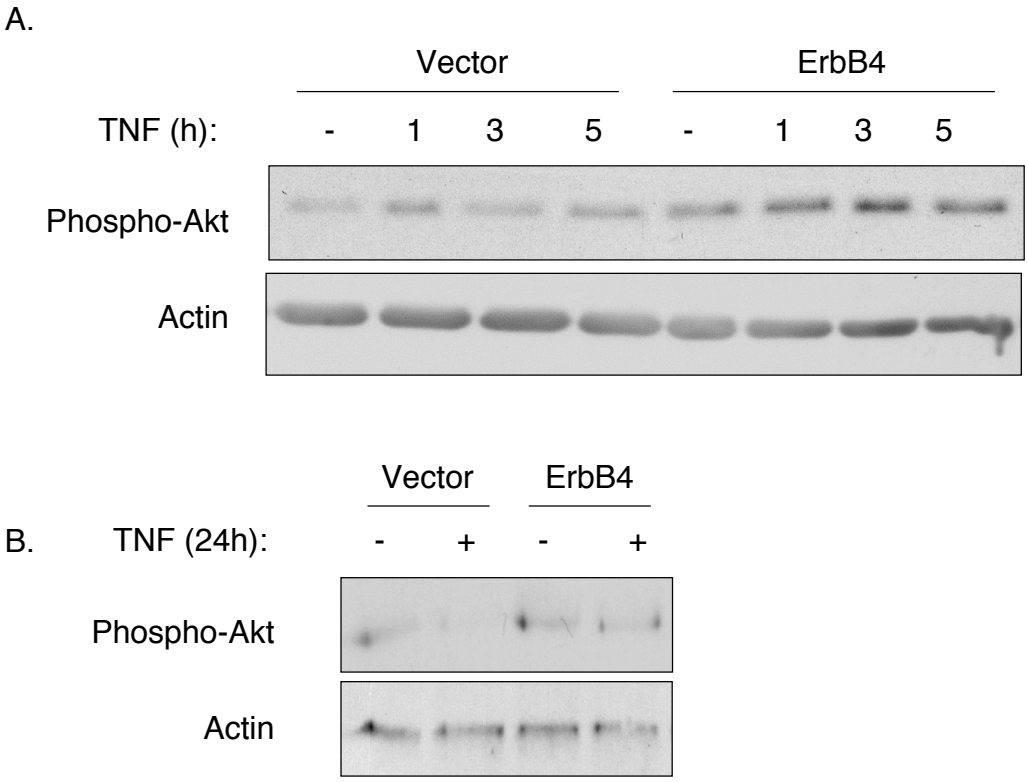
Supplementary figure 4. TNF does not stabilize the ErbB4 protein. ErbB4-overexpressing (JM-a, CYT-2 isoform) cells were preincubated with TNF for 8h and chased with 1 μg/ml TNF for indicated times. ErbB4 protein retention was assessed by Western blot analysis. Graph plots densitometry from 3 independent experiments. *, $p < 0.05$ vs. control.



Supplementary figure 5. Either TNFR1 or TNFR2 is sufficient to mediate TNF-induced ErbB4 accumulation. YAMC, TNFR1$^{-/-}$, or TNFR2$^{-/-}$ mouse colon epithelial cells were treated with 100 ng/ml TNF for 16h. ErbB4 was immunoprecipitated and immunocomplexes subjected to Western blot analysis for ErbB4. Actin blots were performed on input lysate. fl, full-length.



Supplementary figure 6. ErbB4 siRNA effects on YAMC cells are rescued by ErbB4 re-expression. (A) YAMC cells were transfected with non-targeting or ErbB4-specific siRNA and treated with TNF for 16h. ErbB4 expression was determined by Western blot analysis of whole cell lysates. (B) YAMC cells expressing human ErbB4 construct were transfected with the siRNA pool used in our experiments, which primarily (3 of 4 sequences no sequence overlap) targets primarily mouse ErbB4. ErbB4 expression was determined by Western blot. (C) Cells expressing vector or human ErbB4 construct were transfected with anti-mouse ErbB4 siRNA and subjected to wound healing assays. (D) Cells expressing vector or human ErbB4 were transfected and subjected to TUNEL apoptosis assay after 6h TNF exposure. *, $p < 0.05$ vs. all other conditions (no other significant differences).



Supplementary figure 7. ErbB4 expression results in increased Akt phosphorylation. YAMC cells expressing either vector or ErbB4 were treated with TNF for (A) 1-5h or (B) 24h, and whole cell lysates were subjected to Western blot analysis using antibody specific for phosphorylated Akt.