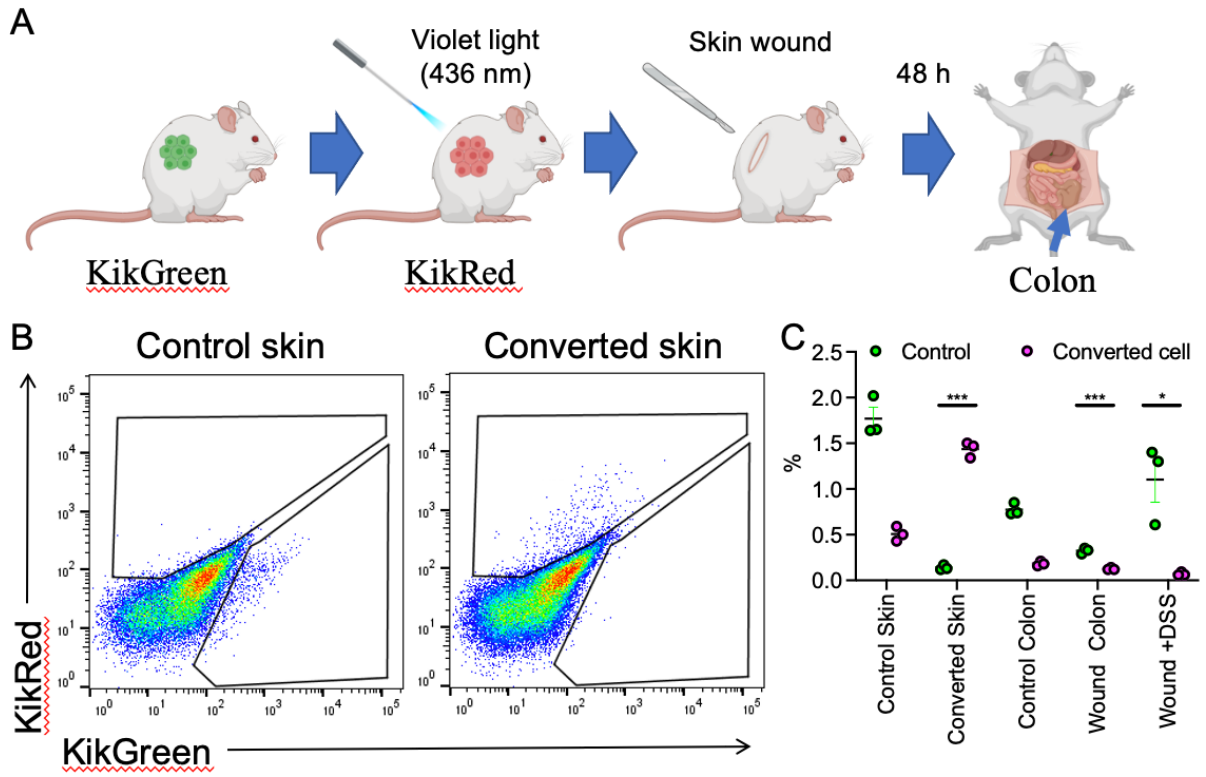
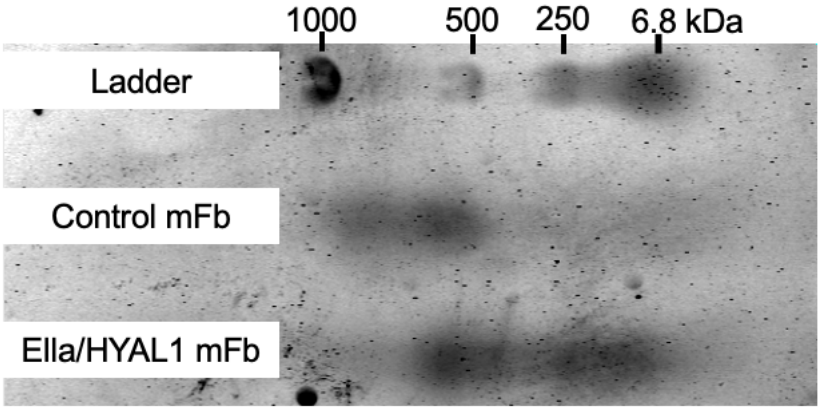
Supplemental Figures



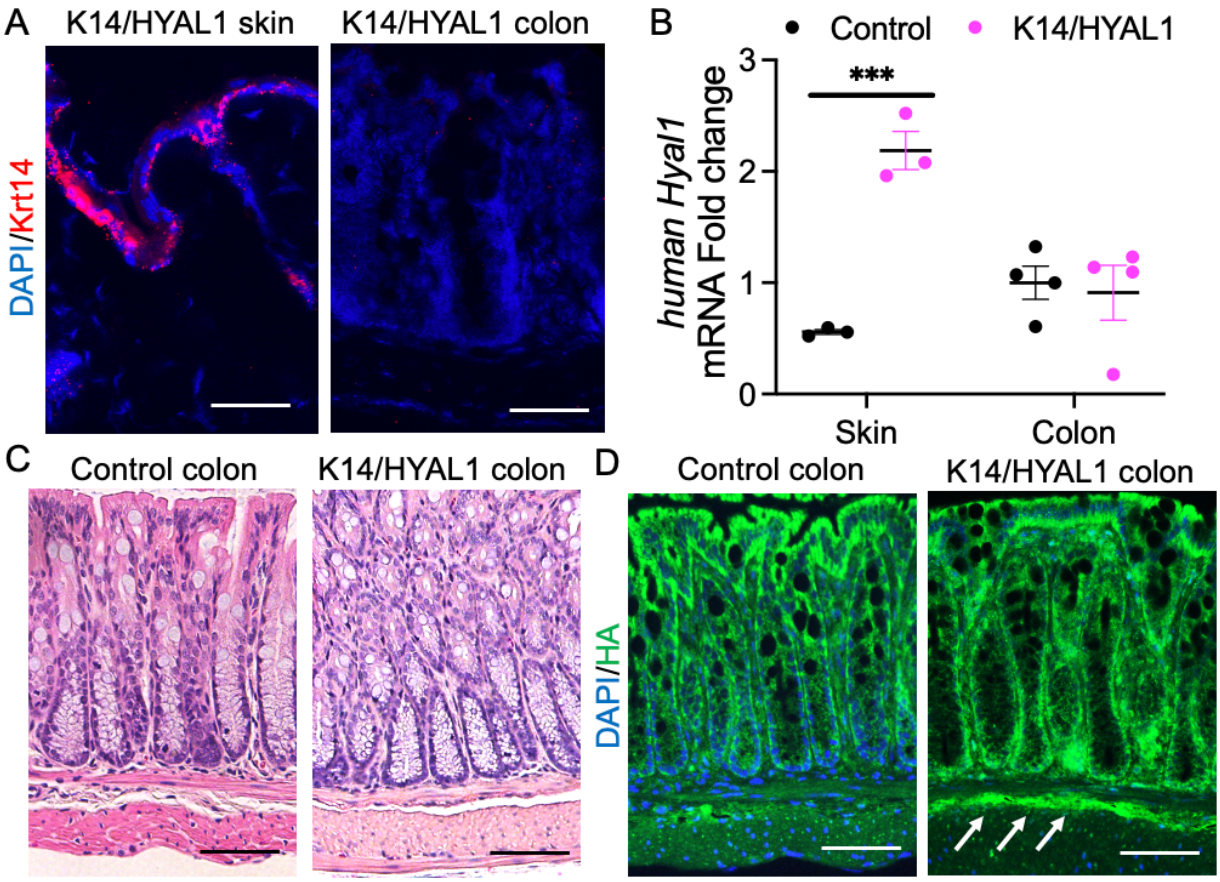
Supplemental Figure 1. Photoconvertable tracking of cells following skin injury

(A) Schematic of photoconversion experiments and cell tracking experiments. The back skin of KikGR mice was irradiated to label only cells of the skin red, and then the back skin injured by aseptic full thickness incisions. Colon and skin were evaluated by FACS 48 hours following skin injury and 7 days DSS treatment. (B) Representative flow cytometry plots of skin after activation showing presence of KikGreen+ to KikRed+ photoconverted cells. (C) Relative abundance in the skin and colon of photoconverted cells from control, wounded, and wounded with colitis mice, P values based on two way ANOVA with correction for multiple comparisons n=3. Error bars indicate mean ± SEM; * P<0.05, ** P < 0.01, *** P<0.001 (t-test).



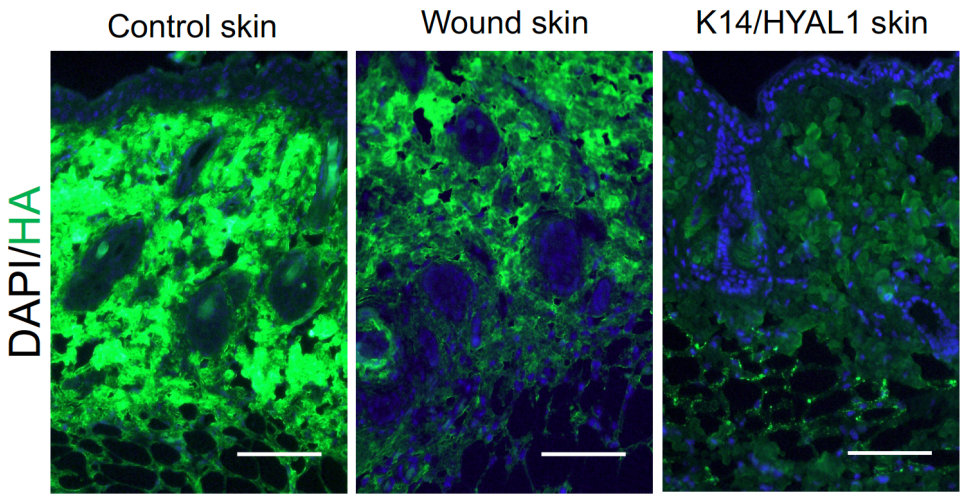
Supplemental Fig. 2. Hyaluronan fraction generated by hHYAL1 overexpressing mFB

Images of HA GEL electrophoresis. HA were extracted from culture supernatant of Control mouse fibroblast and hHYAL1 overexpressing mouse fibroblasts.



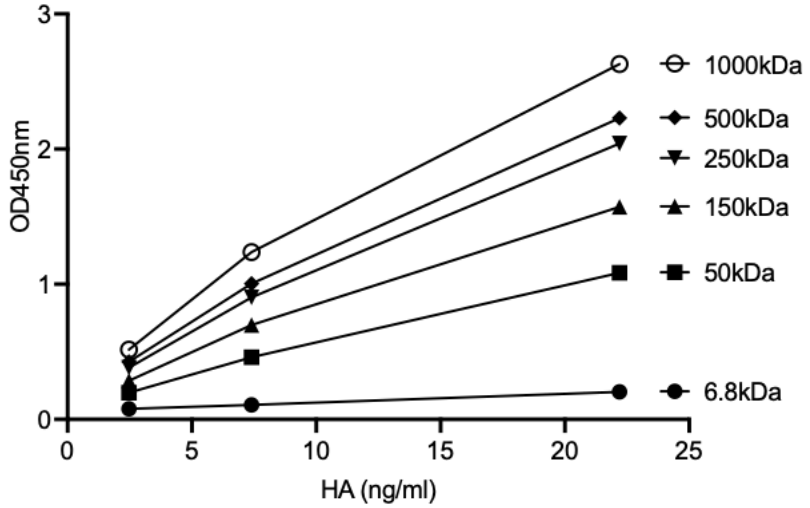
Supplemental Figure 3. Targeted expression of Hyaluronidase-1 in the skin.

(A) In situ hybridization of K14 mRNA shows specific expression in the skin but not the colon of K14/HYAL1 mice. (B) qPCR quantification of Human Hyaluronidase-1 mRNA in the skin and colon. P values based on two way ANOVA with correction for multiple comparisons. n=3 (C) Histological images of colon from K14/HYAL1 and control mice. Tissue was stained with hematoxylin and eosin. (D) Representative images of the colon stained with HABP (green) in control and K14/HYAL1 mice. Scale bar = 50 microns. Error bars indicate mean ± SEM; * $P<0.05$, ** $P < 0.01$, *** $P<0.001$ (t-test)



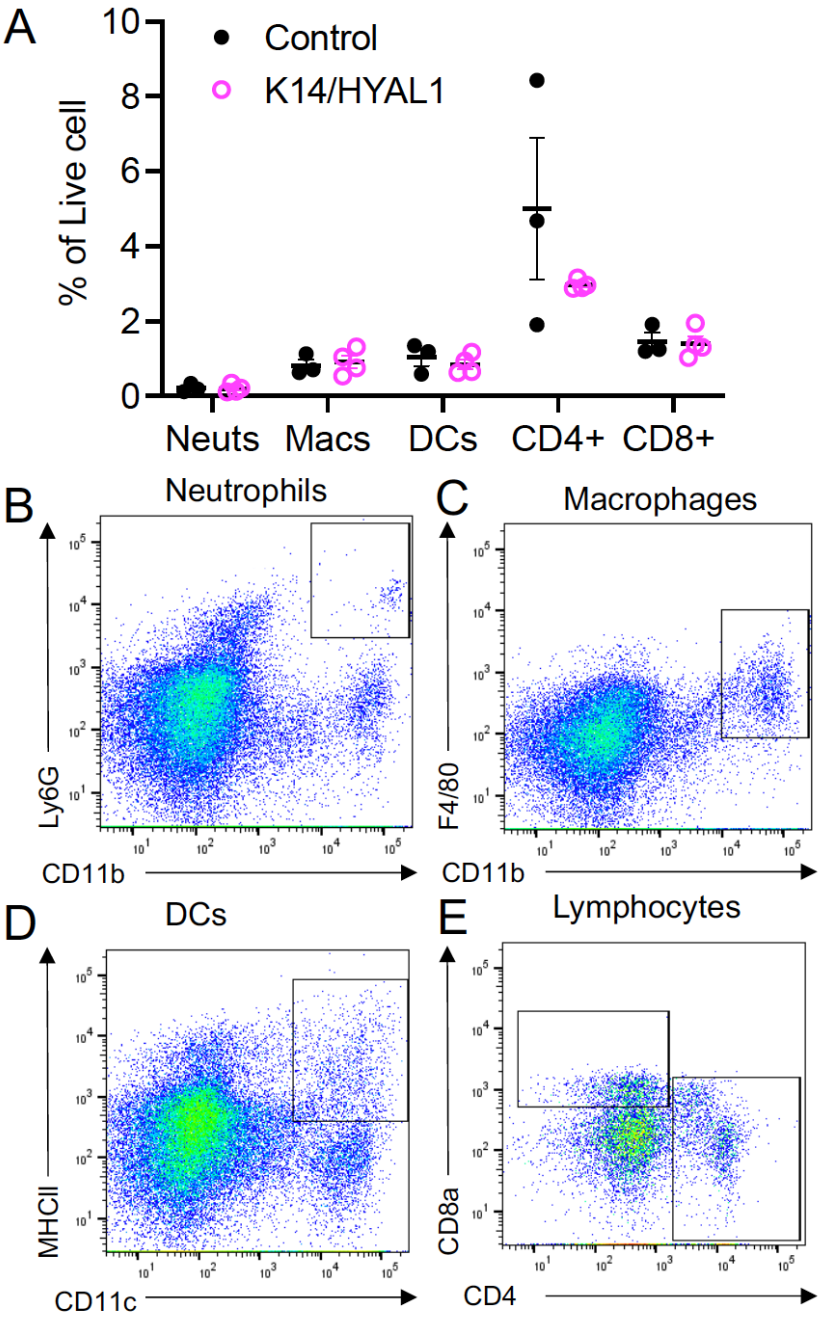
Supplemental Fig. 4. Hyaluronan staining in the skin of control, wounded and K14/HYAL1 mice

Representative images of mouse skin stained with HA-binding protein (green) under control conditions, 48 hours following wounding and in K14/HYAL1 mice. Scale bar = 10 microns.



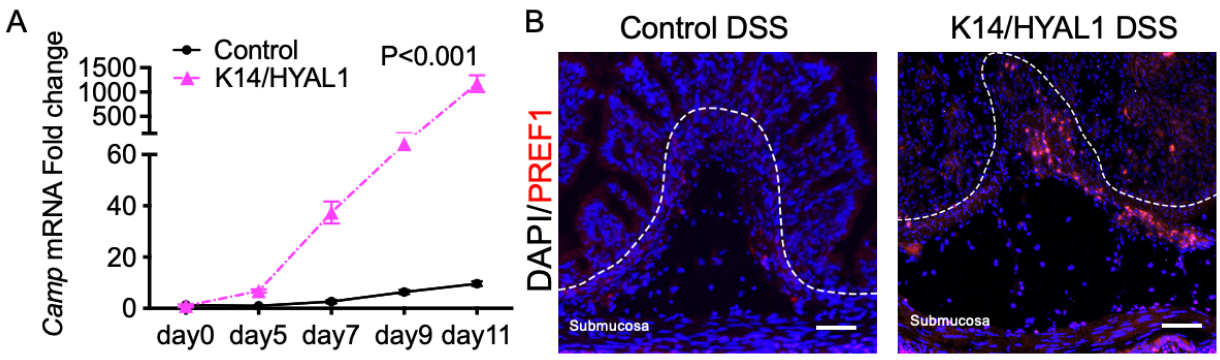
Supplemental Fig. 5. HABP capacity to detect HA is dependent on HA size

HABP ELISA detection standard curves using purified HA of different average molecular weights of 6.8, 50, 150, 250, 500, 1000 kDa HA.



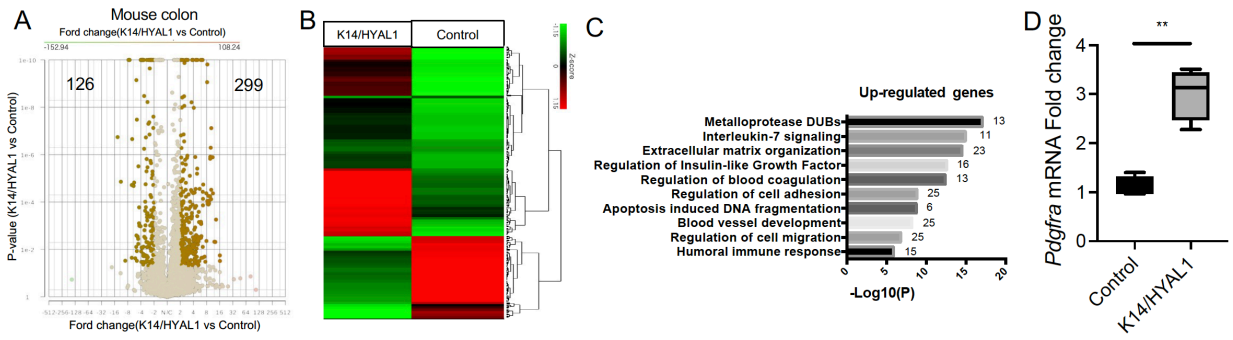
Supplemental Figure 6. Immune cell profiling of the colon in K14/HYAL1 mice

Flow cytometry analysis of single cell suspensions from the colon from control and K14/HYAL1 mice. (A) Numbers represent the percentage of the cells in the indicated gate. Cells were gated as indicated in B to E. P values based on two way ANOVA with correction for multiple comparisons. (B: Neutrophils, C: Macrophages, D: DCs, E: CD4 and CD8).



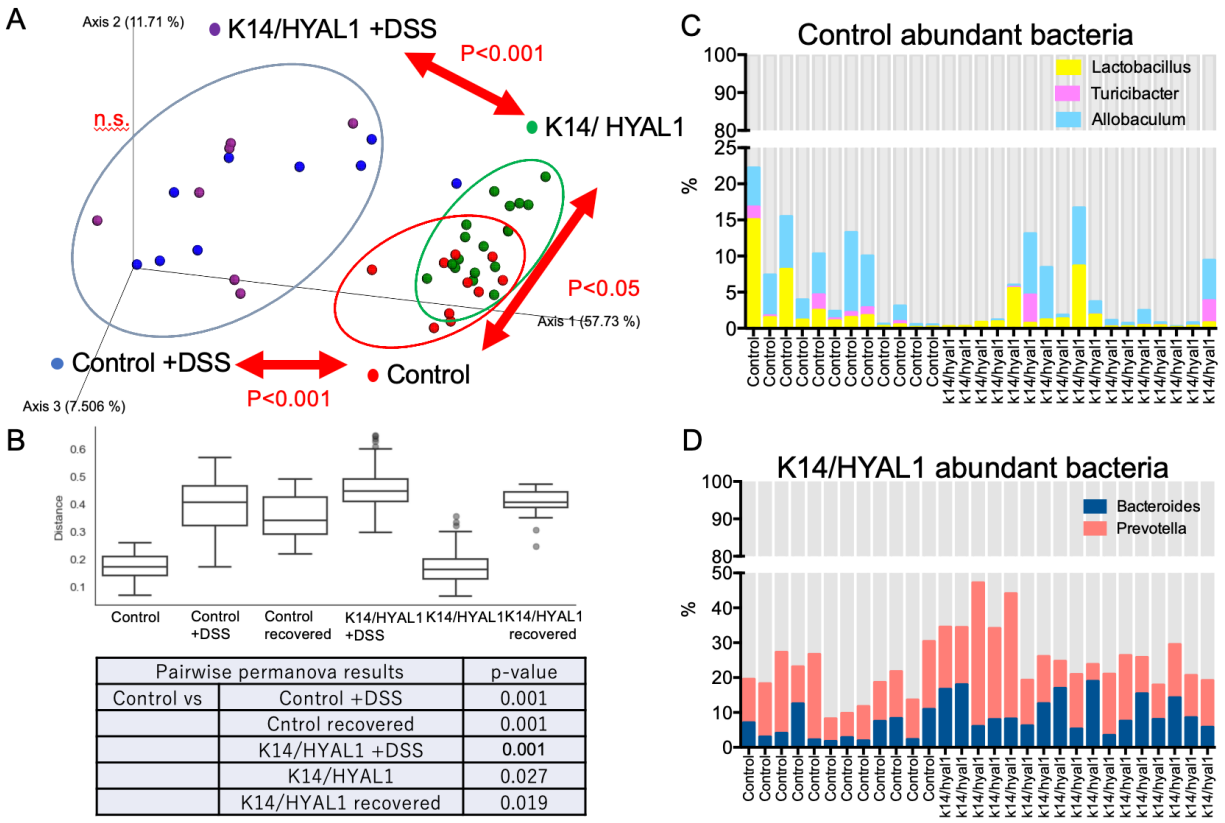
Supplemental Figure 7. Increased expression of *Camp* and Pref1 in the colon of K14/HYAL1 mice after DSS

(A)The expression of *Camp* mRNA in the colon of control and K14/HYAL1 mice. Mice were treated with DSS from day 0 to day 7. (The P value was based on ANOVA n=3) (B) Representative images of mouse colon stained with Pref-1 (red) in control and K14/HYAL1 mice. Scale bar = 50 microns. Error bars indicate mean ± SEM; * P<0.05, ** P < 0.01, *** P<0.001.



Supplemental Figure 8. Digestion of HA in the skin stimulates a transcriptional response in the colon

(A) Volcano plot from RNA Seq of submucosa of colon from Control and K14/HYAL1 mice. (B) Heat map of significantly up or downregulated genes. (C) Gene ontology analysis of upregulated genes in K14/ HYAL1 mice. (D) The expression of mRNA for *Pdgfra*. (The P value was based on t-test, n=3) Error bars indicate mean ± SEM; * P<0.05, ** P < 0.01, *** P<0.001 (t-test).



Pairwise permanova results		p-value
Control vs	Control +DSS	0.001
	Cntrol recovered	0.001
	K14/HYAL1 +DSS	0.001
	K14/HYAL1	0.027
	K14/HYAL1 recovered	0.019

Supplemental Figure 9. Digestion of HA in the skin alters the gut microbiome

16S rRNA amplicon sequencing of stool samples from control and K14/HYAL mice before and after DSS treatment. (Control n=12, K14/HYAL1 n=17) (A) Beta diversity (unweighted Unifrac) principal coordinates analysis (PCoA). (B) Difference in beta diversity (unweighted Unifrac) between groups. (C, D) Taxa plots at level 6. Relative abundance of unique bacteria in Control(C) and K14/HYAL1 (D).