Figure S1 (Related to Figure 1)

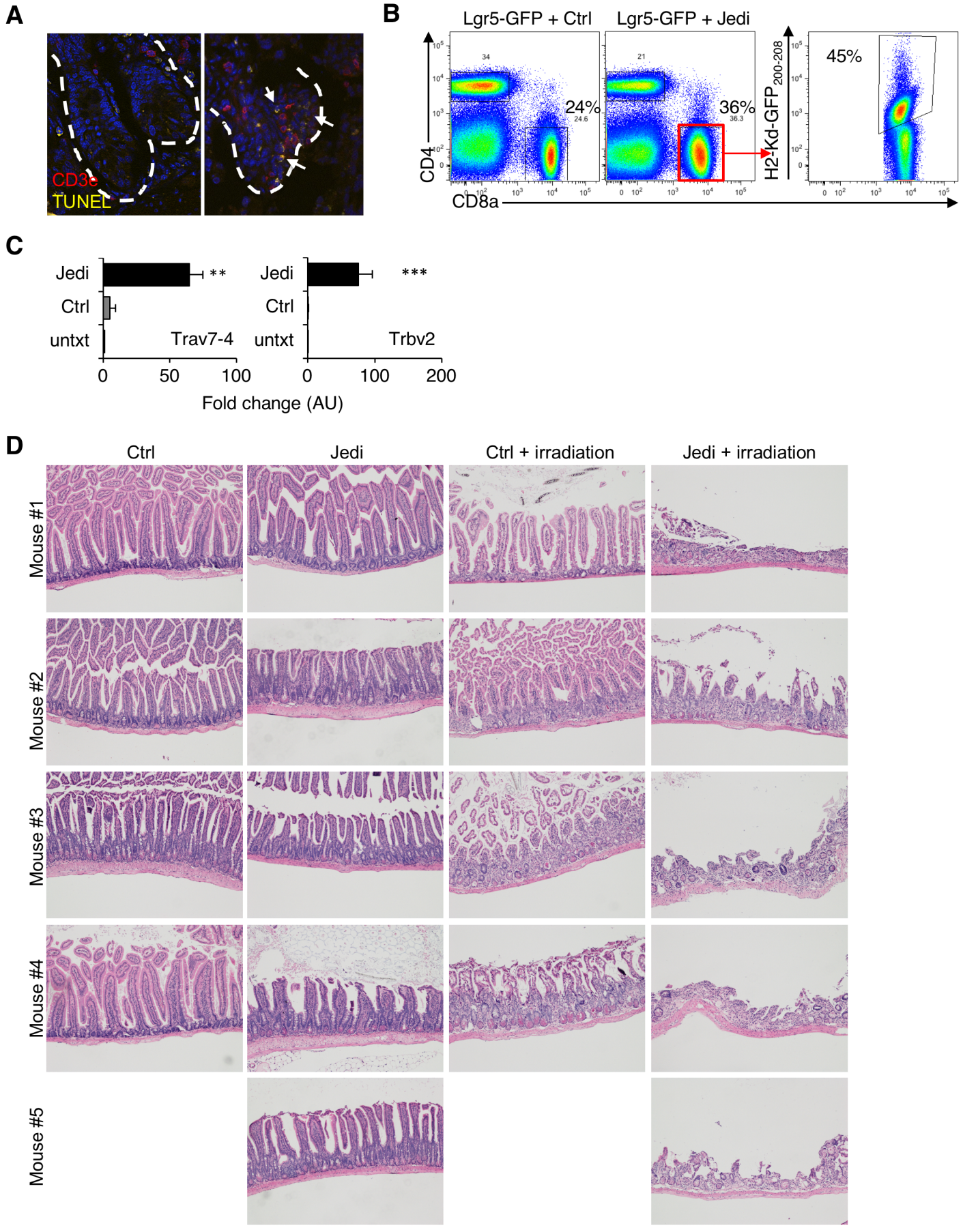


Figure S1 (Related to Figure 1). Gut, ovary and mammary gland stem cells are eliminated by antigen-specific T cells.

(A) Florescent microscopy analysis of the gut of mice 4 days after Control or Jedi T cell adoptive transfer stained for CD3e (red) to mark T cells and TUNEL (yellow) to label apoptotic cells. White arrows point to apoptotic cells. Note that Jedi-treated intestines show abundant apoptotic cells in the crypts in proximity to T cells. Representative images from 3 mice per group are shown.

(B) Flow cytometry analysis of the mesenteric lymph node at 5 days after T cell transfer to measure the frequency of GFP-specific Jedi T cells. Cells were stained for CD4, CD8a and H-2K^{d}-GFP$_{200\text{-}208}$ pentamer.

(C) Reverse transcription quantitative PCR (RT-qPCR) was performed on RNA extracted from the intestine of mice 4 days after Jedi injection to measure expression of the Vα (Trav7-4) and Vβ (Trbv2) chain mRNA specific for the Jedi T cells. Graphs present mean±s.d. relative to untreated mice of 1 experiment (n=3 mice/group).

(D) Representative images showing H&E staining from each mouse in Figure 1D. Briefly, Lgr5-GFP mice received either control (Ctrl) or Jedi T cells and 1 week later half of the mice were irradiated (10Gy) or left untreated. Three days after irradiation, small intestines were harvested. One representative picture is shown per mouse, n=4-5 per group.

Figure S2 (Related to Figure 2)

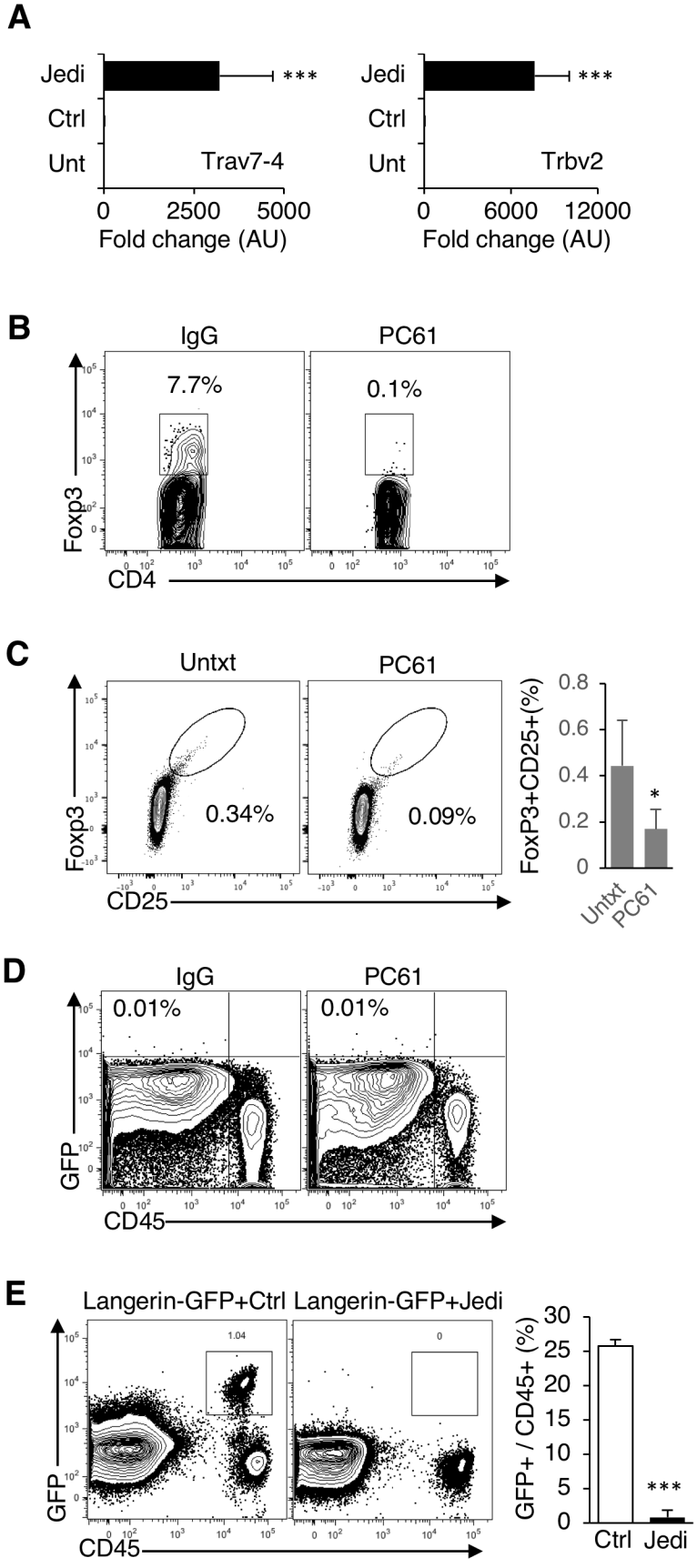


Figure S2. Hair follicle stem cells escape antigen-specific T cell killing.

(A) RT-qPCR was performed on RNA extracted from the skin of Lgr5-GFP injected with Jedi or control T cells to measure expression of the Vα (Trav7-4) and Vβ (Trbv2) chain mRNA specific for the Jedi T cells. Graphs present mean±s.d. relative to untreated (n=3 mice/group).

(B) Lgr5-GFP mice were treated with either anti-CD25 (PC61) antibody or IgG control and 5 days later received Jedi T cells and were vaccinated for GFP. Nine days later mice were sacrificed and Treg depletion was assessed in inguinal lymph nodes by CD4, CD25 and Foxp3 staining. Representative flow cytometry plots are shown. Data are representative of 1 experiments (n=3 mice/group).

(C) Mice were treated with anti-CD25 (PC61) or left untreated and skin was harvested 7 days later and analyzed. Treg depletion was assessed by CD4, CD25 and Foxp3 staining. Representative flow cytometry plots are shown. Graph presents mean±s.d. Data are representative of 1 experiments (n=3 mice/group).

(D) Single cell suspension from intestines from mice in B were analyzed to assess the frequency of GFP+ cells. CD45 was used to stain hematopoietic cells. Representative flow plots are shown.

(E) 7-8 week-old Langerin-GFP mice (in telogen phase) were injected with Jedi or control CD8+ T cells, and vaccinated with GFP. Flow cytometry analysis of the frequency of GFP+ cells in the epidermis 2 weeks after T cell transfer. Cells were stained with CD45 to mark hematopoietic cells and CD11c and MHCII were used to stain for Langerhans cells. Graphs present the mean±s.d. of the frequency of GFP+ cells relative to the total CD45+ live cells. Data are representative of 2 experiments (n=5 mice/group).

***P<0.01 vs Control-treated.

Figure S3 (Related to Figure 3)

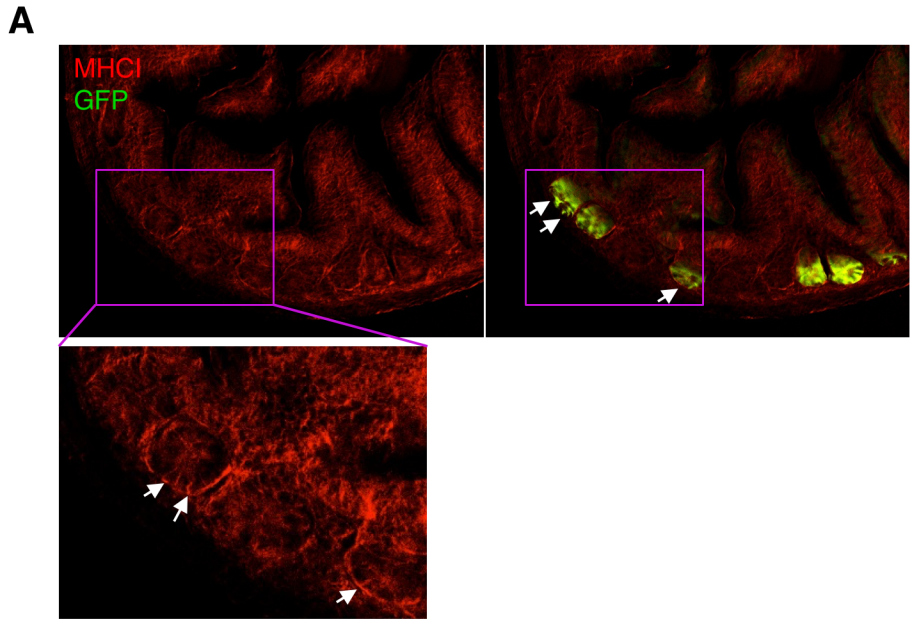


Figure S3 (Related to Figure 3). Intestinal stem cells express MHC class I.

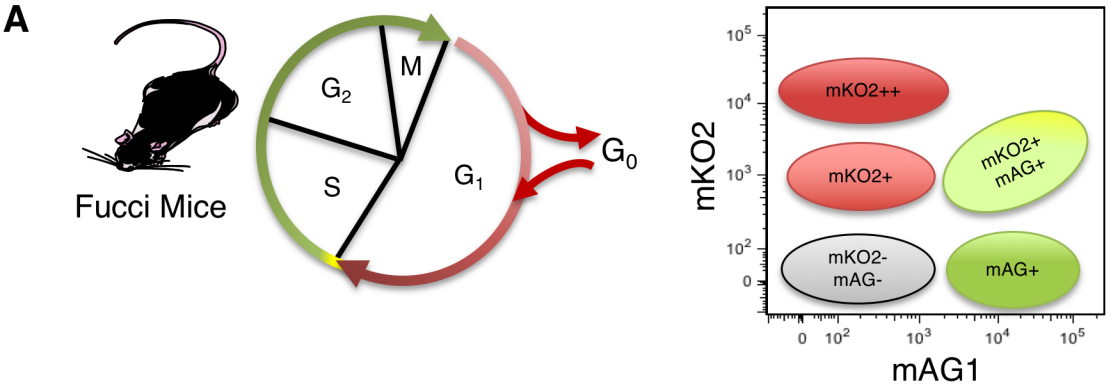
(A) Representative images of small intestines from Lgr5-GFP mice after staining with anti-H2Kd-647 antibody. GFP was directly visualized (n=4).

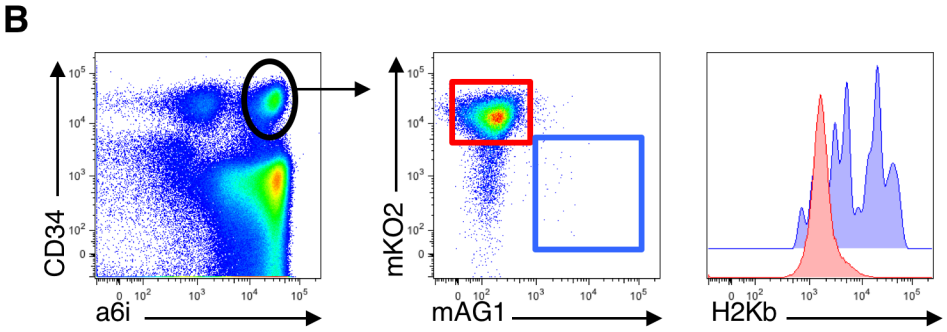
(B) Flow cytometry analysis of NK cell activation shown as Lamp-1 expression in NK cells (CD45+ NK1.1+) in co-culture with HFSCs and keratinocytes. YAC-1 cells were used as a positive control (n=2)

(C) Flow cytometry analysis of NK cell killing of HFSCs and keratinocytes in vitro co-culture. YAC-1 cells were used as controls (n=2).

(D) Flow cytometry analysis of CD45.1 T cells infiltrating the intestine of mice described in Figure 3K. Single cell suspensions from gut were stained with CD3e to label T cells and CD45.1 to label donor T cells (from control and Jedi mice). Representative flow plots are shown (n=3-4).

Figure S4 (Related to Figure 4)





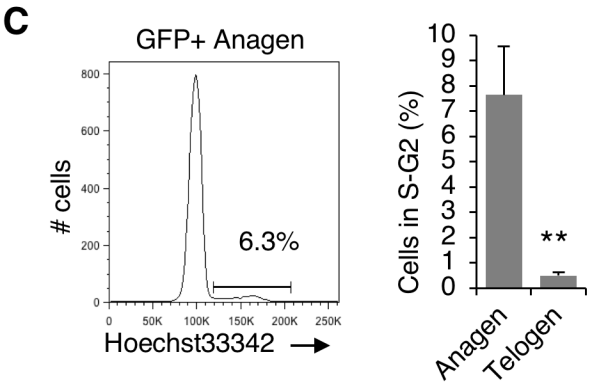


Figure S4 (Related to Figure 4). Downregulated MHC class I is a property of quiescent HFSCs.

(A) Fucci mice express the orange (mKO2) and green (mAG) fluorescent probes under the control of the CAG promoter. mKO2 labels G0 and G1 cells while mAG is visualized during S/G2/M phase (*left*). Right scheme represents a flow cytometry plot showing mKO2 and mAG1 expression that could be observed in any cell type.

(B) Fucci mice were used to assess proliferation in HF cells. Skin of Fucci mice in telogen was processed to obtain a single cell suspension and stained with CD34 and α-6-integrin to label HFSCs, CD45 to label hematopoietic cells, and H2kb antibody for MHC class I. mKO2 positive mAG1 negative labels cells in G0 or G1 and mAG1 positive are cells in cycle. Representative flow cytometry plots are shown (n=5 mice/group).

(C) The skin from Lgr5-GFP mice in anagen (P35) and telogen (P49) were processed to obtain a single cell suspension and stained with Hoechst33342 to assess proliferation. Representative flow cytometry plots are shown. Histograms show GFP+ live (7AAD-negative) cells. Gate in the histogram includes cells in S and G2. Graph presents mean±s.d. of the percentage of cells in S and G2 (n=3 mice/group). **P<0.01

Figure S5 (Related to Figure 5)

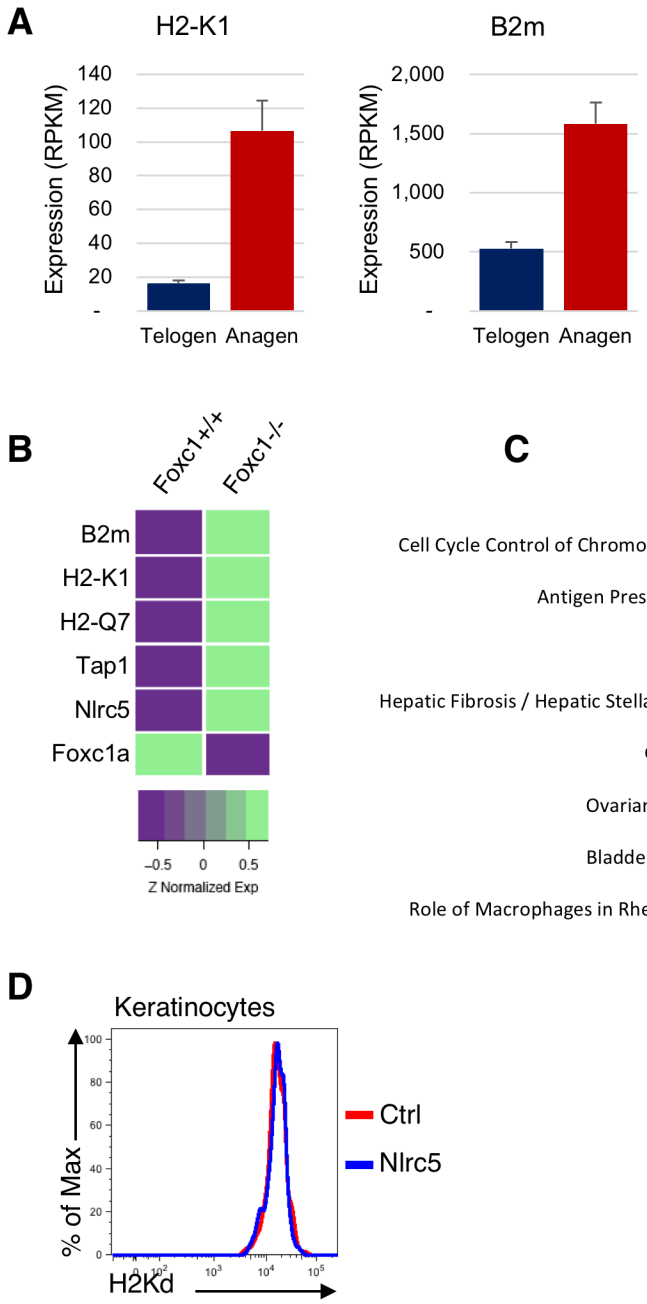


Figure S5 (Related to Figure 5). Nlrc5 is downregulated in quiescent stem cells and its expression restores MHC class I in HFSCs.

(A) Graphs show H2-K1 and B2m expression in Lgr5-GFP+ flow sorted cells in telogen and anagen as measured by RNA-sequencing (n=3-4).

(B) Heatmap shows key differentially expressed genes involved in antigen presentation in RNA-sequencing data from Lay et al. PNAS 2016 (GSE77256), in which HFSCs from Foxc1 deficient mice were compared to HFSCs from littermate controls. Each column shows the mean of all samples. Data is color coded to reflect gene expression Z-scores.

(C) Ingenuity software was used to analyze genes that were statistically different in WT vs Foxc1-/- ($p<0.05$) from Lay et al. Of note, the antigen presentation pathway was the second most altered.

(D) CD34- CD45- interfollicular cells were flow sorted and nucleofected with either a plasmid encoding Nlrc5-GFP fusion protein or GFP alone as a control (Ctrl). Cells were cultured for 36h and stained with H2Kd antibody to determine MHCI expression. Histograms show DAPI- (live) GFP+ cells, representative histogram is shown.

Figure S6 (Related to Figure 6)

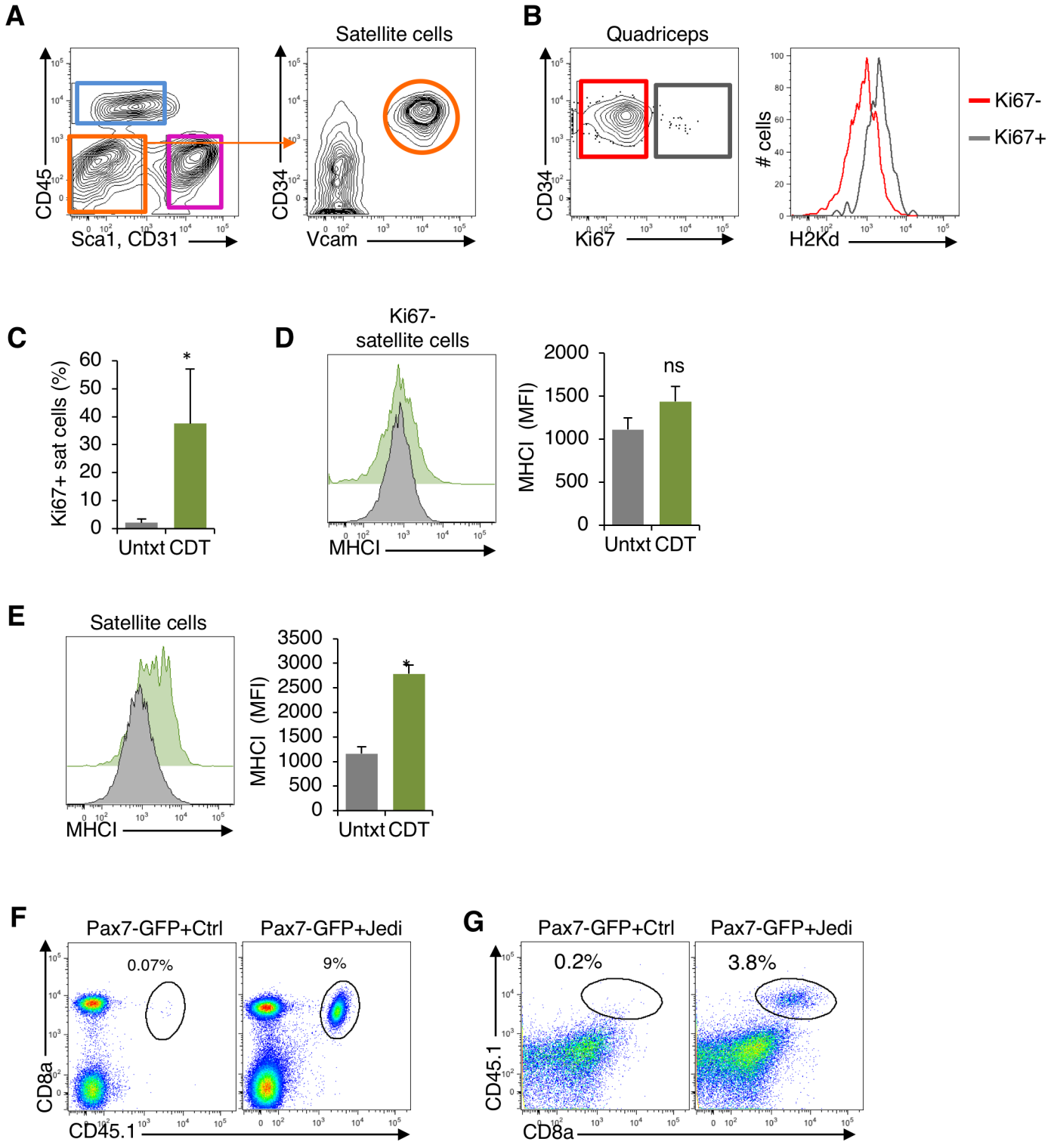


Figure S6 (Related to Figure 6). Immune evasion is a property of muscle quiescent stem cells.

(A) Representative flow cytometry plots showing gating strategy for satellite cells in muscle. Satellite cells are identified as DAPI- Sca1- CD45- CD31- CD34+ Vcam+.

(B) Ki67 staining was assessed in satellite cells from quadriceps. Satellite cell population was divided into Ki67-negative (red) and Ki67-positive (dark grey) and H2Kd intensity was assessed in these populations separately. Representative flow cytometry plots are shown from 2 experiments (n=4 mice/group).

(C) Graph presents the mean±s.d. of the frequency of Ki67+ cells relative to the total live satellite cells from two-month old wild-type mice 40 h after injection of cardiotoxin (CDT) compared to untreated (Untxt) littermates (n=3 mice/group). *P<0.05.

(D) Representative flow cytometry histogram showing mean fluorescent intensity (MFI) of MHC class I expression in satellite cells injected with PBS or cardiotoxin (CDT). Graph presents the mean±s.d. of the MFI MHC class I (n=3 mice/group). n.s.= non-significant statistical difference.

(E) Representative flow cytometry histograms showing MFI of MHC class I expression in total satellite cells from animals in (C). Graph presents the mean±s.d. of the MFI of MHC class I (n=3 mice/group). *P<0.05 vs stallite cells from CDT-treated mice.

(F) Representative flow cytometry plots showing CD45.1+ CD8+ T cells from donor mice (control or Jedi) in the popliteal lymph nodes in Pax7-CreERT2xCAG-DsRed-GFP mice from Fig. 6I-J (n=5 mice/group from 2 experiments).

(**G**) Representative flow cytometry plots showing CD45.1 CD8 T cells (donor T cells) infiltrating the muscle in Pax7-CreERT2xCAG-DsRed-GFP mice from Fig. 6I-J. The flow plots show cells after gating on DAPI- CD45+ cells.