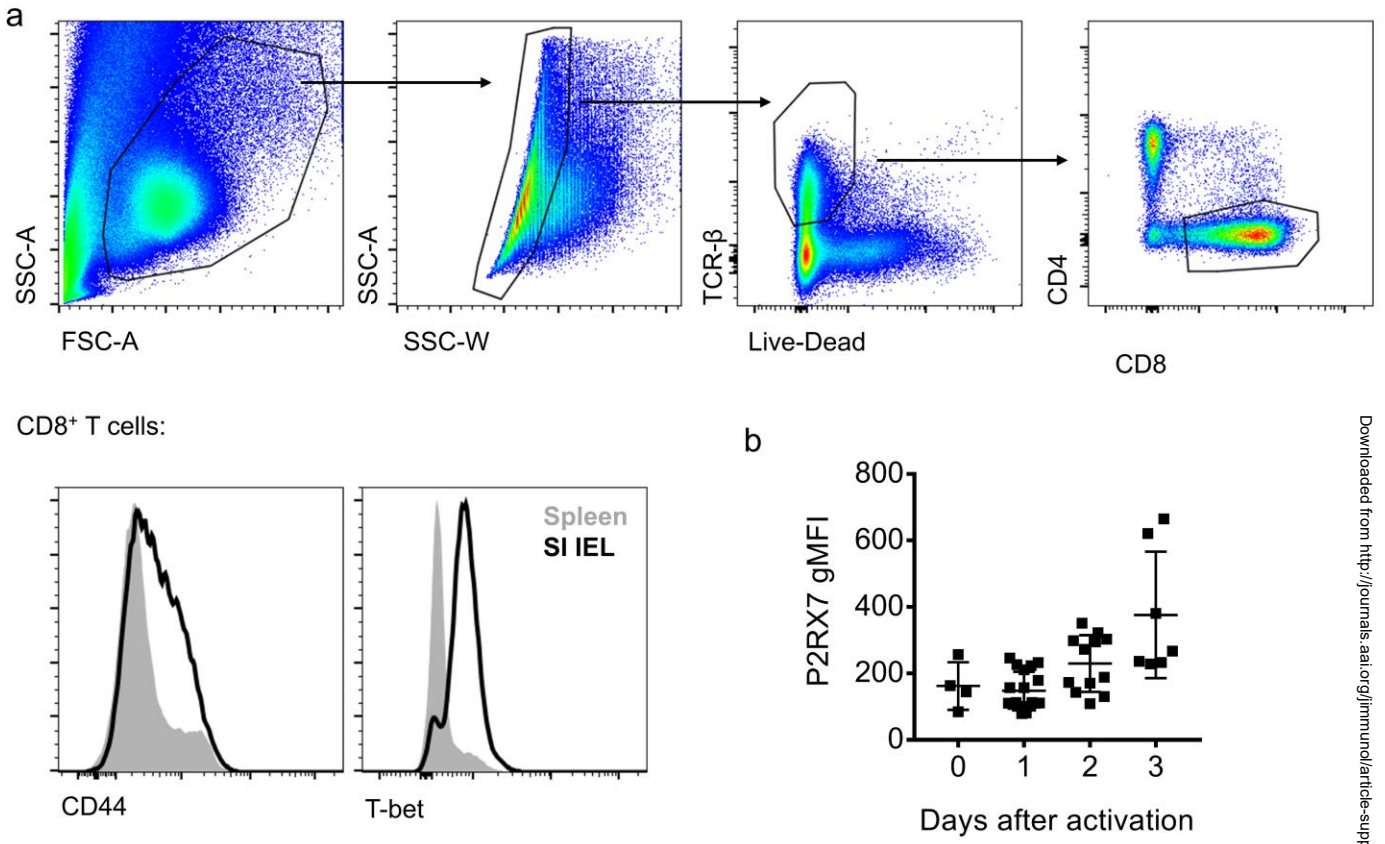

Fig. S1. Characterization of polyclonal small intestine CD8⁺ T cells and kinetics of P2RX7 expression after cognate antigen stimulation. (a) On the top panel, a gating strategy to define polyclonal CD8⁺ T cells, and in the bottom left, representative histograms showing expression of CD44 and T-bet in spleen versus small intestine IEL CD8⁺ T cells. (b) Spleen naïve P14 CD8⁺ T cells were stimulated *in vitro* with gp33 + IL-2. The kinetics of P2RX7 expression levels was followed in these cells for the first 3 days after activation. Data are from 3 independent experiments, n=4-14 per experimental group.

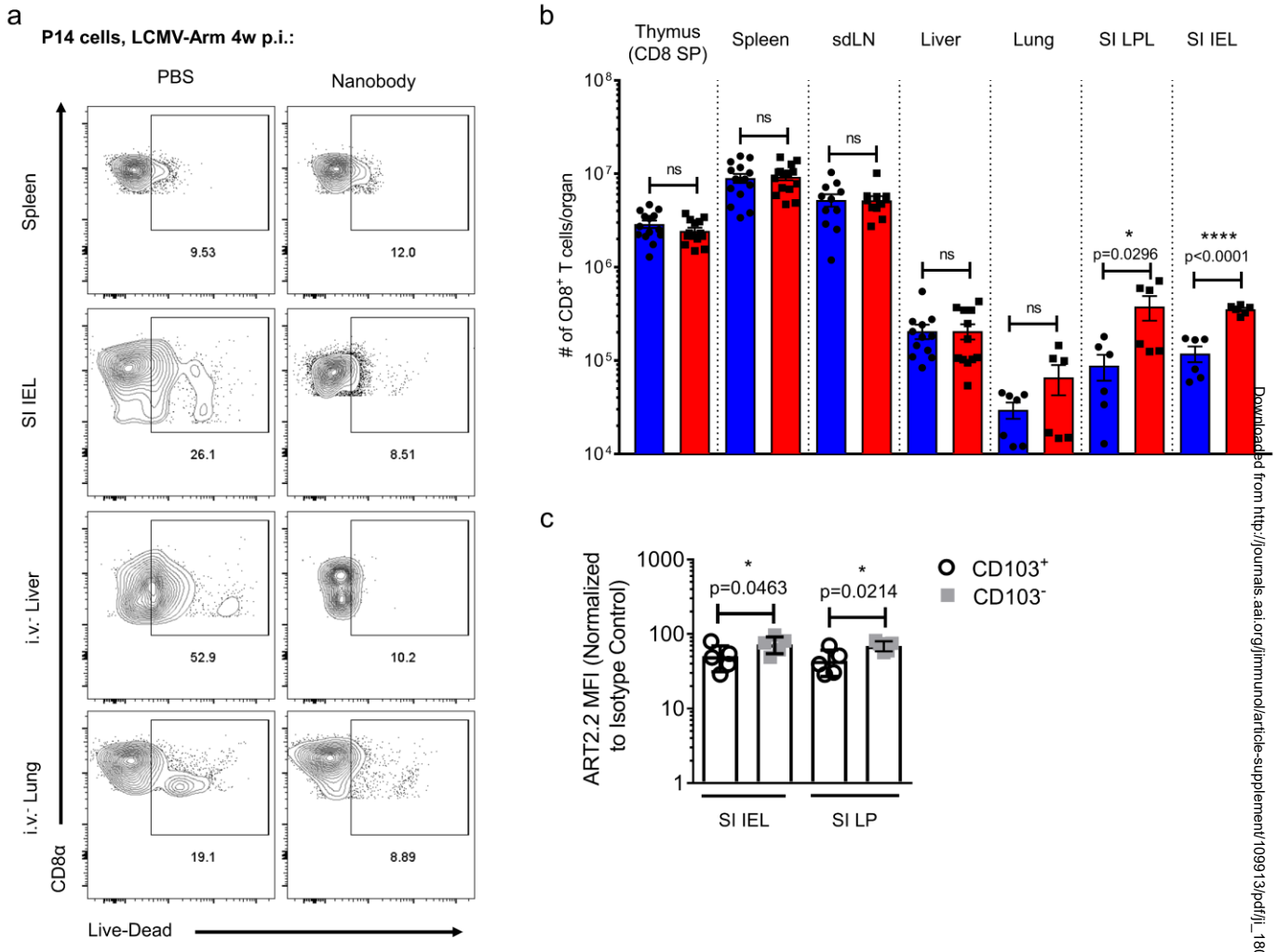

Fig. S2. ARTC2.2 blockade improves recovery of polyclonal CD8⁺ T cells and T_{RM} cell subsets in non-lymphoid tissues. (a) P14 memory cells were isolated from the indicated tissues, after i.v. PBS or Nanobody injection. Representative flow cytometry plots indicating the percentages of dead (Live-Dead+) P14 cells in the indicated tissues are shown. (b) Polyclonal CD8⁺ T cells were isolated from the indicated tissues, with pre-harvest treatment with PBS (blue bars) or Nanobody (red bars). The numbers of CD8⁺ T cells per organ are represented. (c) P14 memory cells isolated from the small intestine IEL and LPL. The expression levels of ARTC2.2 in CD103⁺ versus CD103⁻ T_{RM} cells were measured in both organs. Data are representative from 3-4 independent experiments, n=5-15 per experimental group.

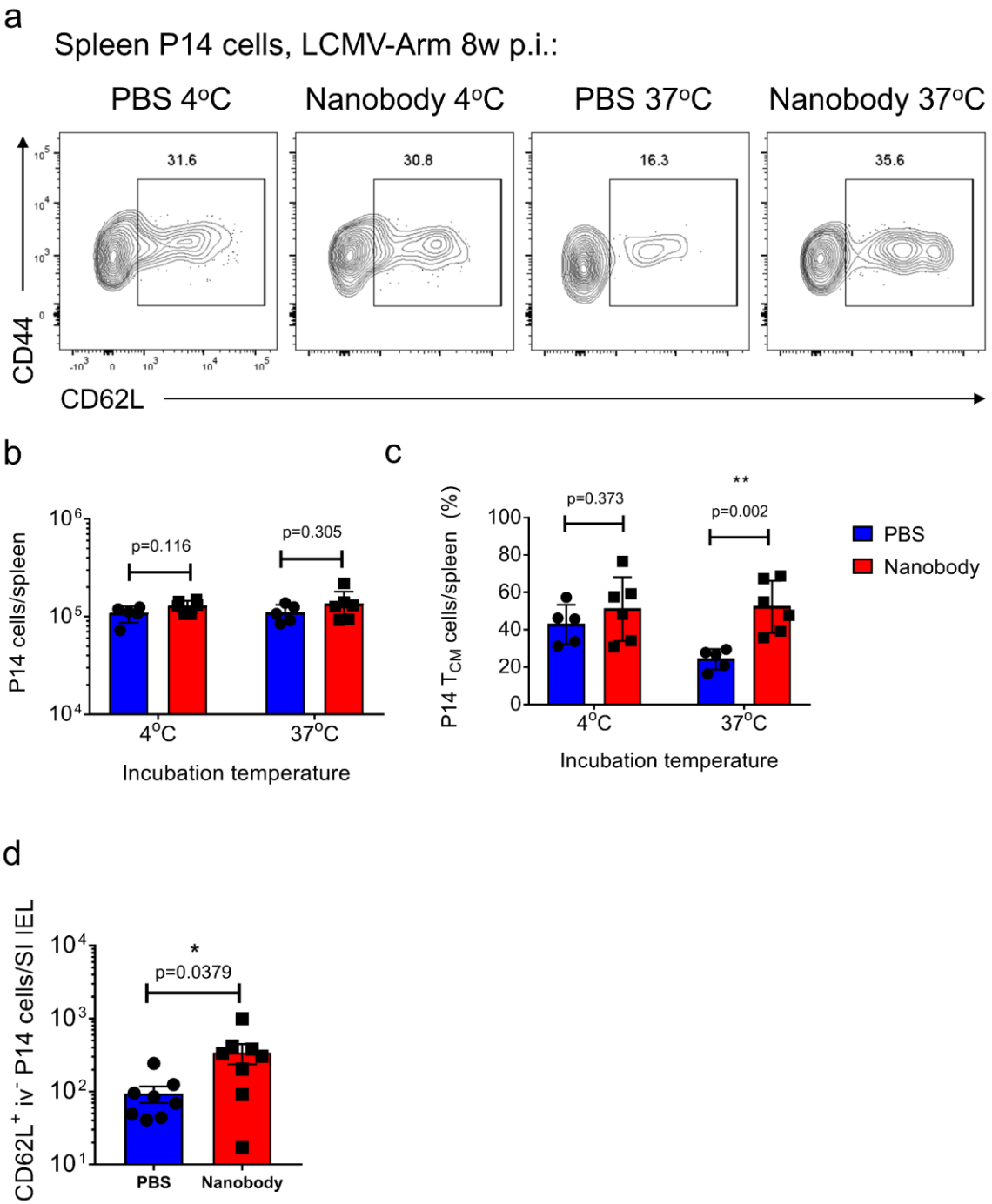

Fig. S3. ARTC2.2 blockade preserves CD62L expression in T_{CM} cells upon 37°C incubation. (a-c) Spleen P14 memory cells were isolated from mice treated with PBS or Nanobody. After processing, each spleen cell suspension was split in two; one half was incubated for 1h at 4°C, and the other half was incubated for 1h at 37°C. After this period, the percentages of $CD44^+CD62L^+$ $CD8^+$ T cells (T_{CM} cells) were assessed by flow cytometry. (a) Representative flow cytometry plots showing expression of CD44 and CD62L in the indicated experimental groups. (b) Spleen P14 cell numbers of PBS- or Nanobody-treated mice, with incubations at 4°C or 37°C. (c) Spleen T_{CM} P14 cell percentages of PBS- or Nanobody-treated mice, with incubations at 4°C or 37°C. (d) SI IEL P14 memory cells were isolated from mice treated with PBS or Nanobody. The numbers of $CD62L^+$ SI IEL P14 cells were then quantified. Data are from 3 independent experiments, n=5-6 per experimental group.

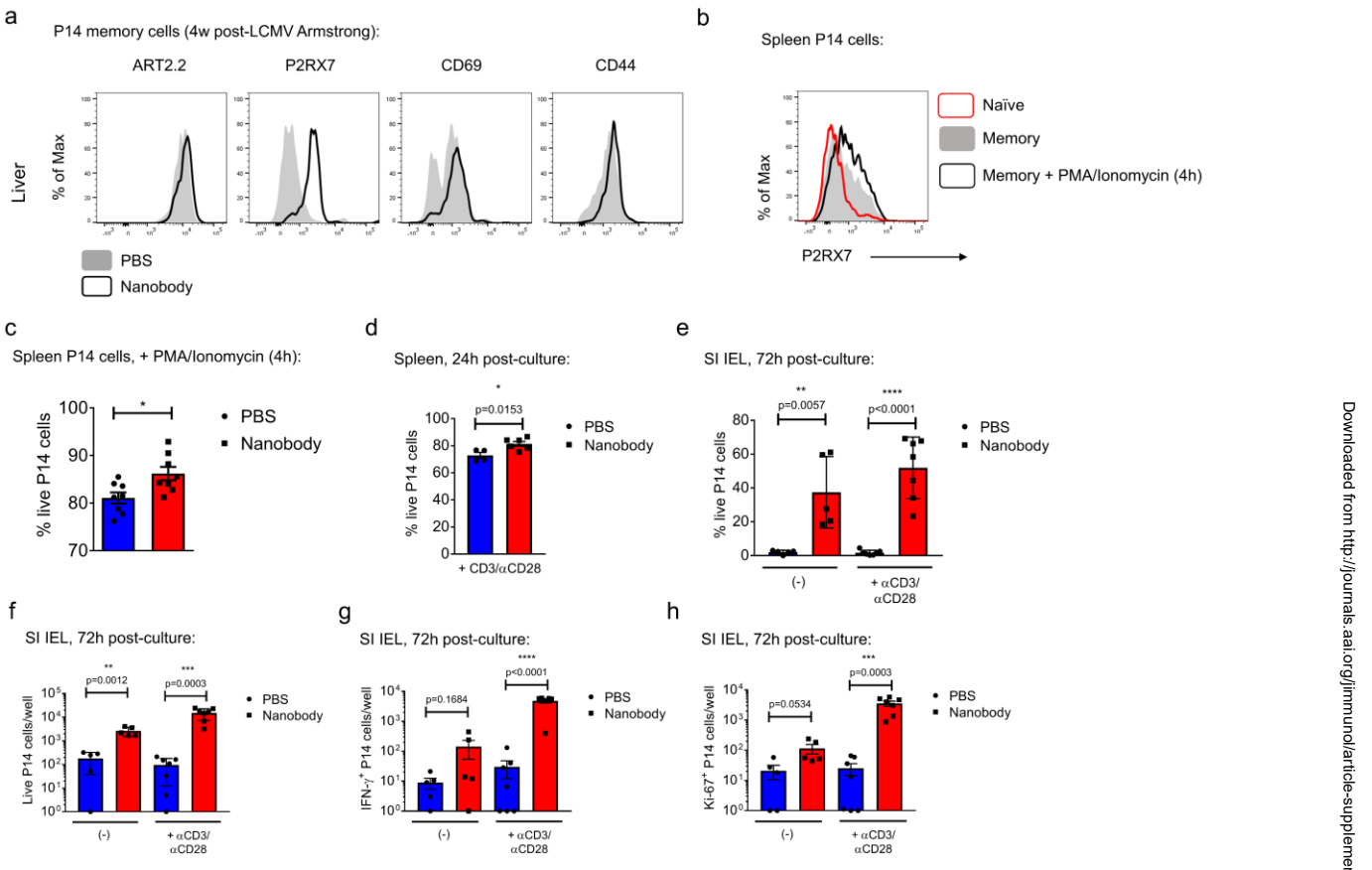

Fig. S4. ARTC2.2 blockade preserves the phenotype and function of SI IEL T_{RM} cells. (a) Representative histograms showing expression levels of ARTC2.2, P2RX7, CD69 and CD44 of liver (i.v.$^-$) P14 cells from PBS- or Nanobody-treated mice. (b) Spleen P14 cells from Nanobody-treated mice were cultured for 4h with PMA/Ionomycin. The expression levels of P2RX7 were then assessed, comparing to *ex vivo* memory or naïve P14 cells. (c-h) P14 memory cells from the spleen or SI IEL were isolated from PBS- or Nanobody-treated mice and cultured *in vitro* as described in Fig.3b. (c) Percentages of live spleen P14 cells per well after 4h of PMA/Ionomycin stimulation. (d) Percentages of live spleen P14 cells per well after 24h of aCD3/aCD28 stimulation. (e) Percentages of live SI IEL P14 cells after 72h of *in vitro* culture without any stimulation (RPMI) or in the presence of αCD3/αCD28. (f) Numbers of live SI IEL P14 cells/well after 72h of *in vitro* culture without stimulation or in the presence of αCD3/αCD28. (g,h) Numbers of IFN-γ$^+$ (g) and Ki-67$^+$ (h) SI IEL P14 cells/well after 72h of *in vitro* culture with RPMI or αCD3/αCD28. Data are from 2-3 independent experiments, n=4-6 per experimental group.