

Supp. Fig. 1. **A**. Sorting strategy for isolation of human ILCs. ILC1 cells (I: Lin-CD127+CRTH2-c-Kit-NKp44-), ILC2 cells (II: Lin-CD127+CRTH2+), and NKp44- ILC3 cells (III: Lin-CD127+CRTH2-c-Kit+NKp44-) were sorted by FACS from PBMCs as described in the Methods. **B**. Expression of ST2 on human peripheral blood ILCs. In a subset of experiments, an aliquot of sorted ILCs was stained for ST2. **C**. Expression of ST2 on the three ILC subsets, as quantified by geometric mean fluorescence index. Combined data of four independent experiments and subjects are shown.

\* p<0.05 (ILC2 vs. ILC1, ILC3 vs. ILC1).



Supp. Fig. 2. RA induces cytokine production in human ILCs in a dose-dependent manner. Concentrations of IL-5, IL-13, and IFN- $\gamma$  were measured in culture supernatants of ILC2 and ILC3 cells incubated with the indicated stimuli. Cytokine data were normalized to 2,000 ILCs per 200 µl culture volume. Combined data of seven independent experiments and subjects are shown.

\* p < 0.05 (cultures with IL-2 + 50 nM RA vs. cultures with IL-2 + 0.5 nM RA).



Supp. Fig. 3: RA acts synergistically with IL-2, but not with IL-12 or IL-7, to induce production of IFN- $\gamma$  in human ILC1 and ILC3 cells. Concentrations of IFN- $\gamma$  were measured in culture supernatants of ILC1 and ILC3 cells incubated with the indicated stimuli. Cytokine data were normalized to 2,000 ILCs per 200 µl culture volume. Combined data of seven independent experiments and subjects are shown.

\* p<0.05 (cultures with cytokine + RA vs. cultures with cytokine alone).

Supp. Fig. 4



Supp. Fig. 4. IL-2 acts synergistically with RA, as well as with known activating cytokines, to induce cytokine production in human ILCs. Concentrations of cytokines were measured in culture supernatants of ILC1 and ILC2 cells incubated with the indicated stimuli. **A**. Production of IFN- $\gamma$  in ILC1 cells. **B**. Production of IL-5 and IL-13 in ILC2 cells. Cytokine data were normalized to 2,000 ILCs per 200 µl culture volume. Combined data of four independent experiments and subjects are shown.

\* p < 0.05 (cultures with IL-2 + other cytokine vs. cultures with IL-2 + RA).

Supp. Fig. 5



Supp. Fig. 5. RA induces expression of integrin  $\alpha 4\beta 7$  on human ILCs in a dose-dependent manner. Expression of  $\alpha 4\beta 7$  was measured on ILC2 and ILC3 cells incubated with the indicated stimuli. Combined data of seven independent experiments and subjects are shown.

\*\* p<0.01 (cultures with IL-2 + 50 nM RA vs. cultures with IL-2 + 0.5 nM RA).

Supp. Fig. 6

Unstim

11.2 2\*RA

PP.

11-7

Unstim

11.2

ŗ,×



Supp. Fig. 6. A. RA acts synergistically with activating cytokines to induce expression of integrin  $\alpha 4\beta 7$  on human ILCs. Expression of  $\alpha 4\beta 7$  was measured on ILCs incubated with the indicated stimuli. Combined data of seven independent experiments and subjects are shown. B. RA acts synergistically with activating cytokines to induce expression of integrin  $\alpha 4\beta 1$  on human ILCs. Expression of  $\alpha 4\beta 1$  was measured on ILCs incubated with the indicated stimuli. Combined data of four independent experiments and subjects are shown. C. RA inhibits expression of CLA on human ILCs. Expression of CLA was measured on ILCs incubated with the indicated stimuli. Combined data of four independent experiments and subjects are shown. \* p<0.05, \*\* p<0.01 (cultures with cytokine + RA vs. cultures with cytokine alone).

11-7

1×

1.2 2\*RA

8A

1/1

Unstim

Supp. Fig. 7



Supp. Fig. 7. Effect of IL-2, RA (50 nM) and 1,25D3 (50 nM) on survival and proliferation of human ILCs. A. Numbers of plated ILCs per variable at the start of culture. **B**. Numbers of live cells per variable after 5 days of culture. Live cells were gated and counted by flow cytometry. **C**. Representative example of expression of the proliferation marker Ki-67 in ILCs. **D**. Expression of Ki-67 was measured in ILCs incubated with the indicated stimuli, and the frequency of Ki-67-expressing cells is shown as percentage of live ILCs. Combined data of four independent experiments and subjects are shown.



Supp. Fig. 8: Cytokine production in human ILC2 cells is induced by RA, but not by RAR inverse agonist (RAi) or RAR antagonist (RARant.). Concentrations of IL-5 and IL-13 were measured in culture supernatants of ILC2 cells incubated with the indicated stimuli. Cytokine data were normalized to 2,000 ILCs per 200 µl culture volume. Combined data of four independent experiments and subjects are shown.