**Supplementary Materials**:

**Figure S1**. Selective inhibition of RORγ by VTP-938.

**Figure S2**. Gating strategy for CD4+ T cells in lung-draining lymph nodes.

**Figure S3**. Identification by CyTOF of cell populations in the lungs of OVA-challenged mice.

**Figure S4**. Gating strategy for IL-17-producing cells in the lung.

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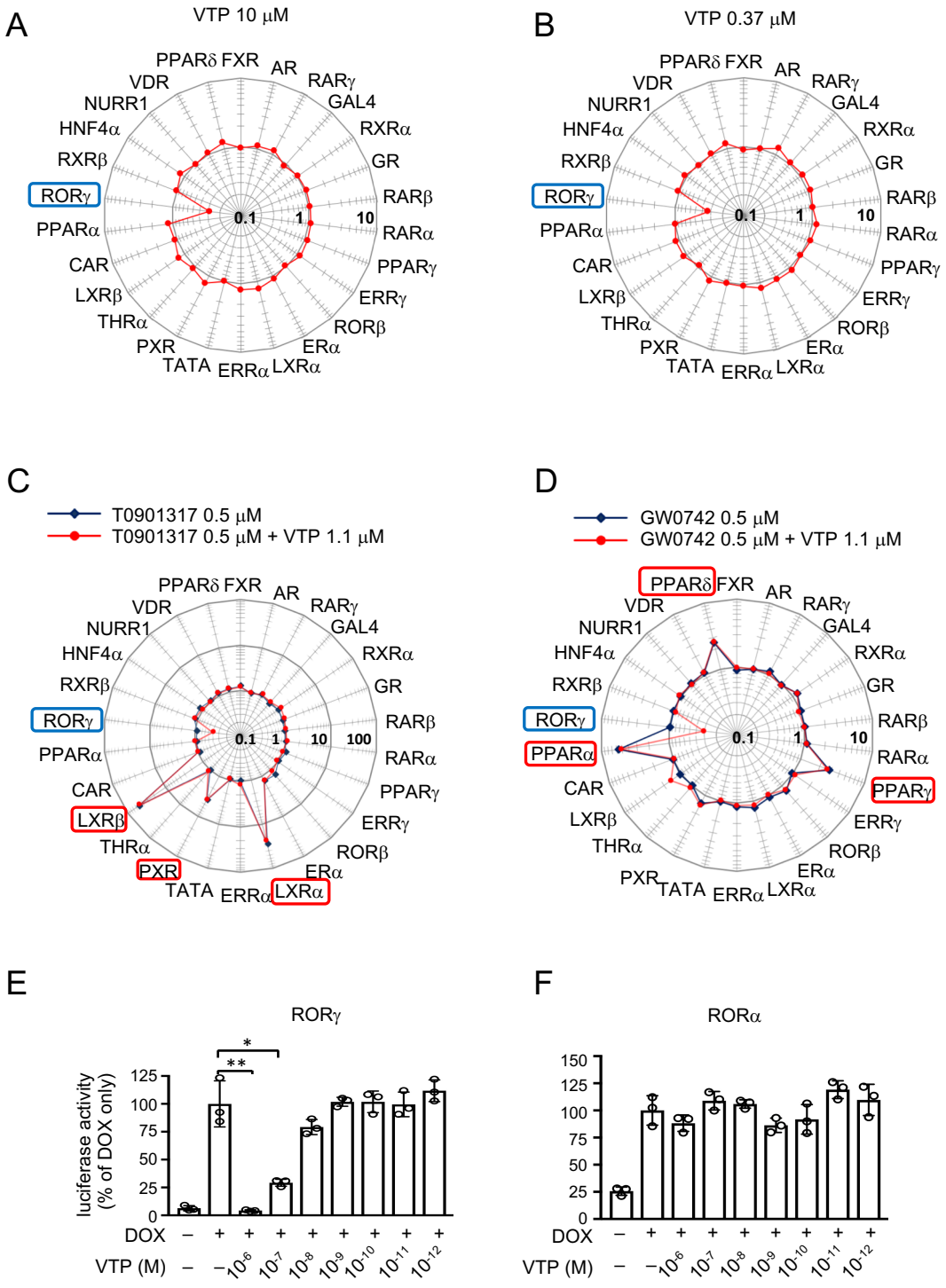
**Figure S6**. Effect of VTP given prior to allergen challenge on three consecutive days.

**Figure S7**. Identification by CyTOF of cell populations in the lungs of HDE-challenged mice.

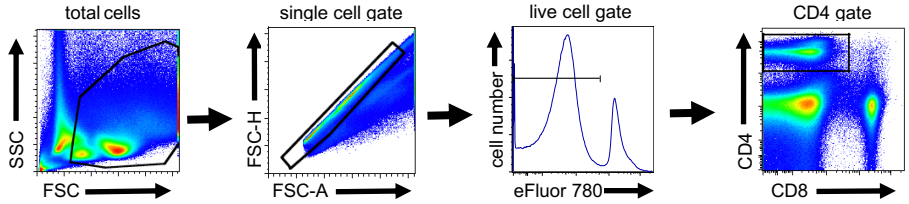
**Figure S8**. Plasma concentrations of VTP-938.

**Table S1**. List of antibodies used for CyTOF experiments.



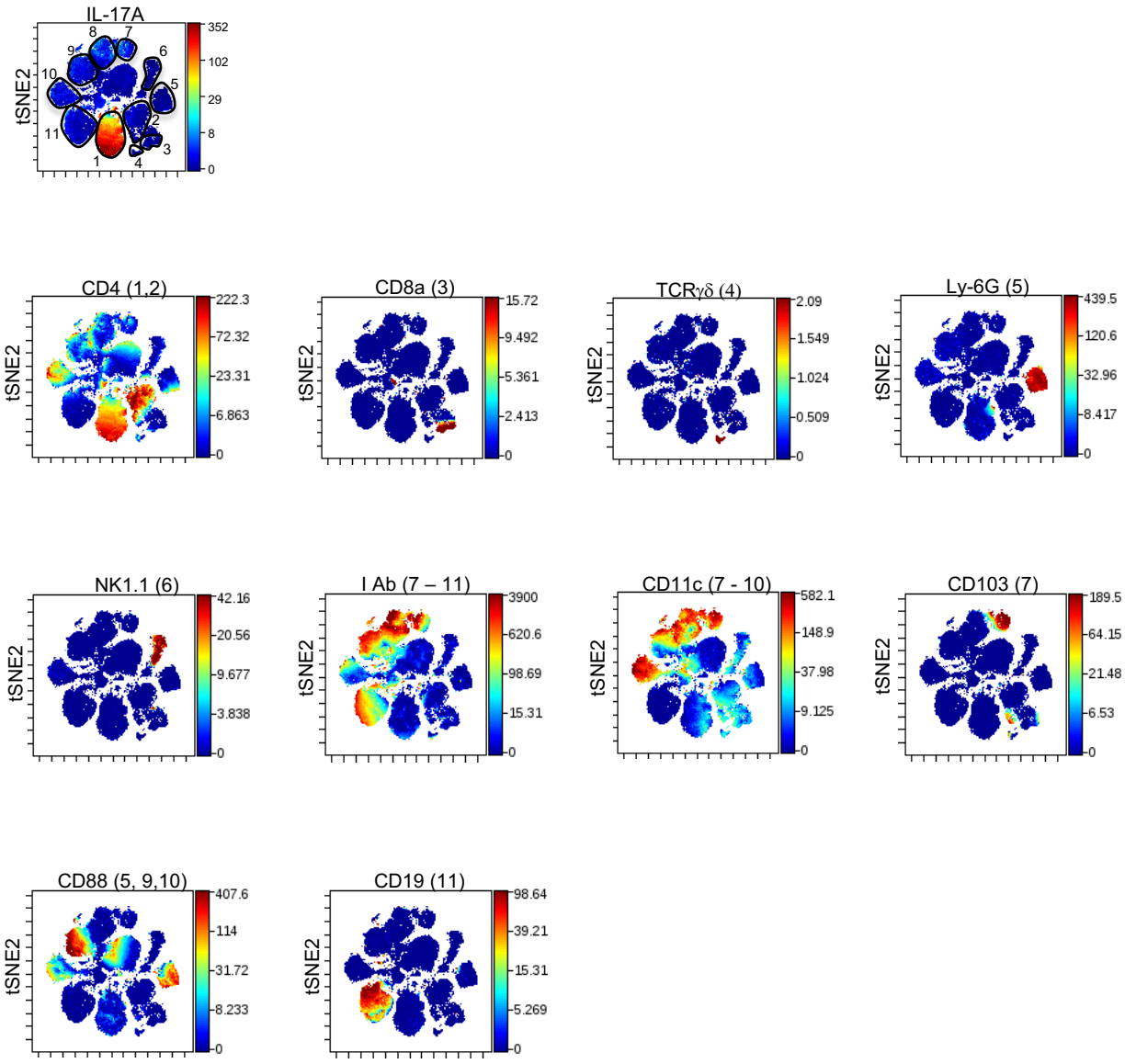

**Supplementary Figure S1. Selective inhibition of RORγ by VTP-938**. (**A, B**) Trans-Factorial assay assessing the effect of VTP (10 or 0.37 μM) on the activity of 24 human nuclear receptors. VTP only inhibits RORγ. (**C**) Trans-Factorial assay examining the effect of VTP (1.1 μM) on the activation of nuclear receptors by the LXR agonist T0901317. "1", indicates VTP has no effect; "10", 10-fold increase; "0.1", 10-fold decrease; "100", 100-fold increase. VTP has no effect on the activation of LXRα, PXR, and LXRβ. (**D**) Trans-Factorial assay examining the effect of VTP (1.1 μM) on the activation of nuclear receptors by the PPAR agonist GW0742. VTP has no effect on the activation of PPARα, PPARβ, and PPARγ. (**E, F**) Doxycycline (DOX)- and ROR-dependent activation of a RORE-driven Luciferase (LUC) reporter in CHO RORγ-Tet-On cells (E) and CHO RORα-Tet-On cells (F) in the presence of different VTP concentrations. Shown is percent LUC activity relative to cells treated with DOX plus vehicle (DMSO) alone (bar 2). *P<0.05; **P<0.01, as determined by 2-way ANOVA.

Supplementary Figure S2



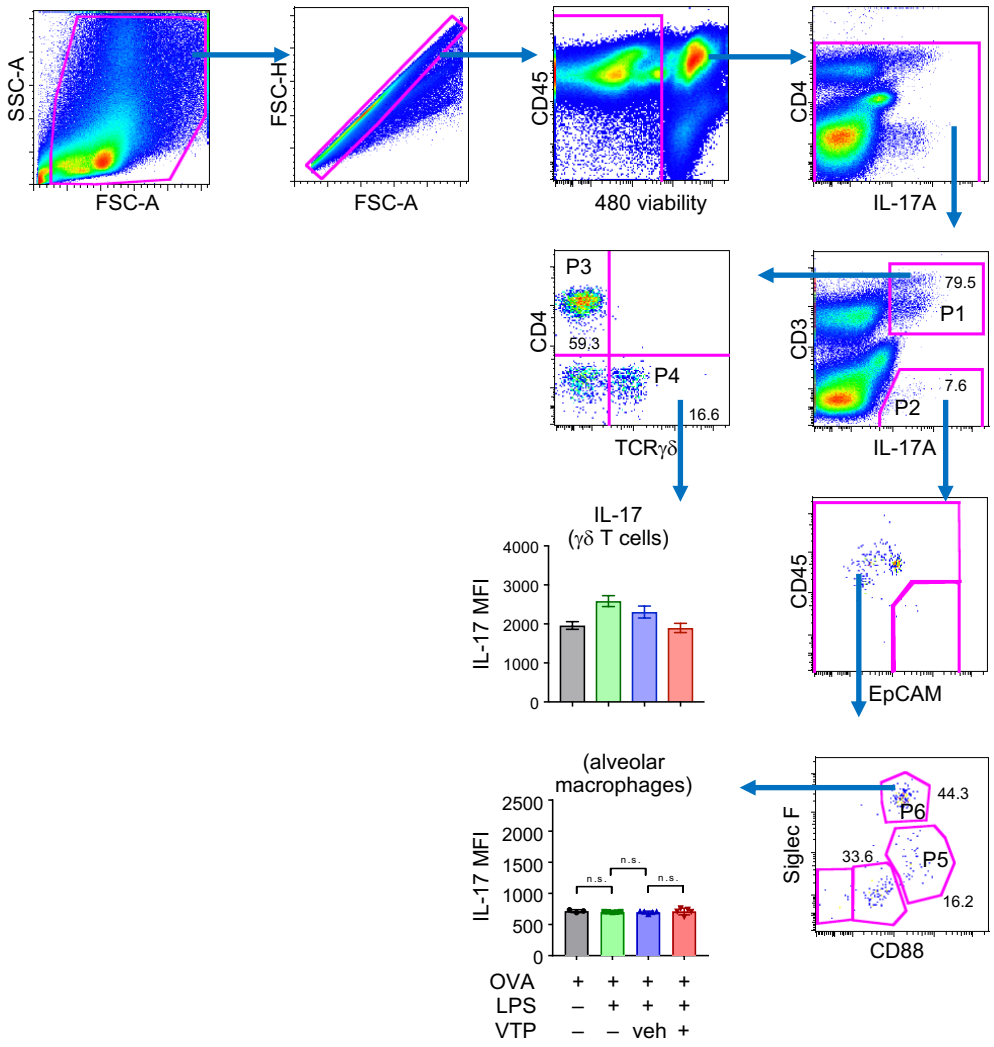

**Supplementary Figure S2**. Gating strategy for CD4⁺ T cells in lung-draining lymph nodes. Gates are based on forward and side scatter (FSC and SSC), single cells, live cells, and CD4 and CD8 staining.

Supplementary Figure S3



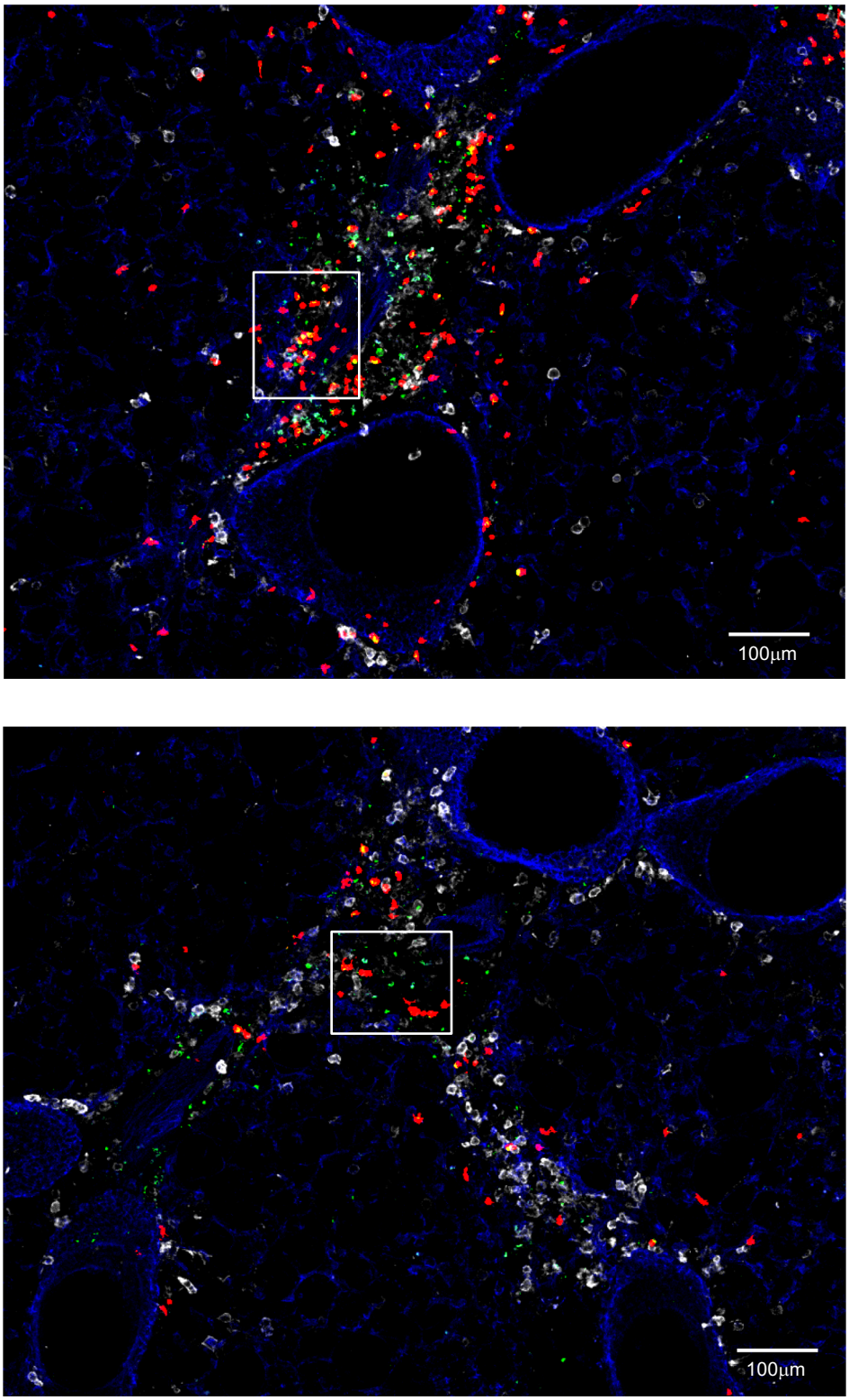

**Supplementary Figure S3**. **Identification by CyTOF of cell populations in the lungs of OVA-challenged mice.** (Top) IL-17 staining of cells within cell populations identified as Th17 cells (1), other CD4$^+$ T cells (2), CD8$^+$ T cells (3), TCR$\gamma\delta^+$ T cells (4), neutrophils (5), NK T cells (6), CD103$^+$ DCs (7), CD11b$^+$ DCs (8), interstitial macrophages (9), alveolar macrophages (10) and B cells (11). Also shown are staining for molecules that contribute to the identification of these cell populations.

Supplementary Figure S4



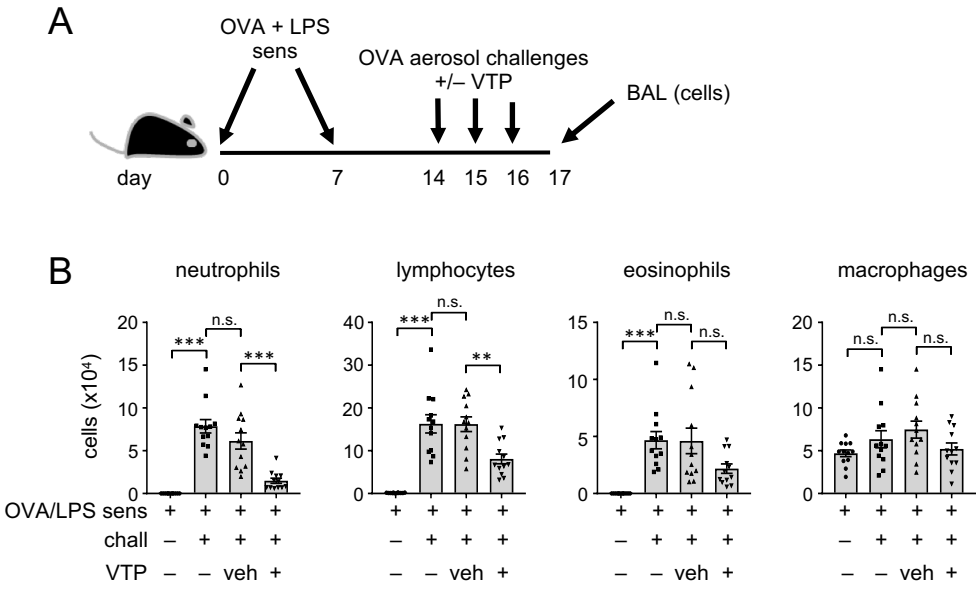

**Supplementary Figure S4**. **Gating strategy for IL-17-producing cells in the lung.** Shown are gating strategies to identify IL-17$^+$CD3$^+$ T cells (P1), IL-17$^+$ non-T cells (P2), IL-17$^+$CD4$^+$TCR$\alpha\beta^+$ T cells (P3) IL-17$^+$CD4$^-$TCR$\gamma\delta^+$ T cells (P4), interstitial macrophages (P5) and alveolar macrophages (P6).

Supplementary Figure S5



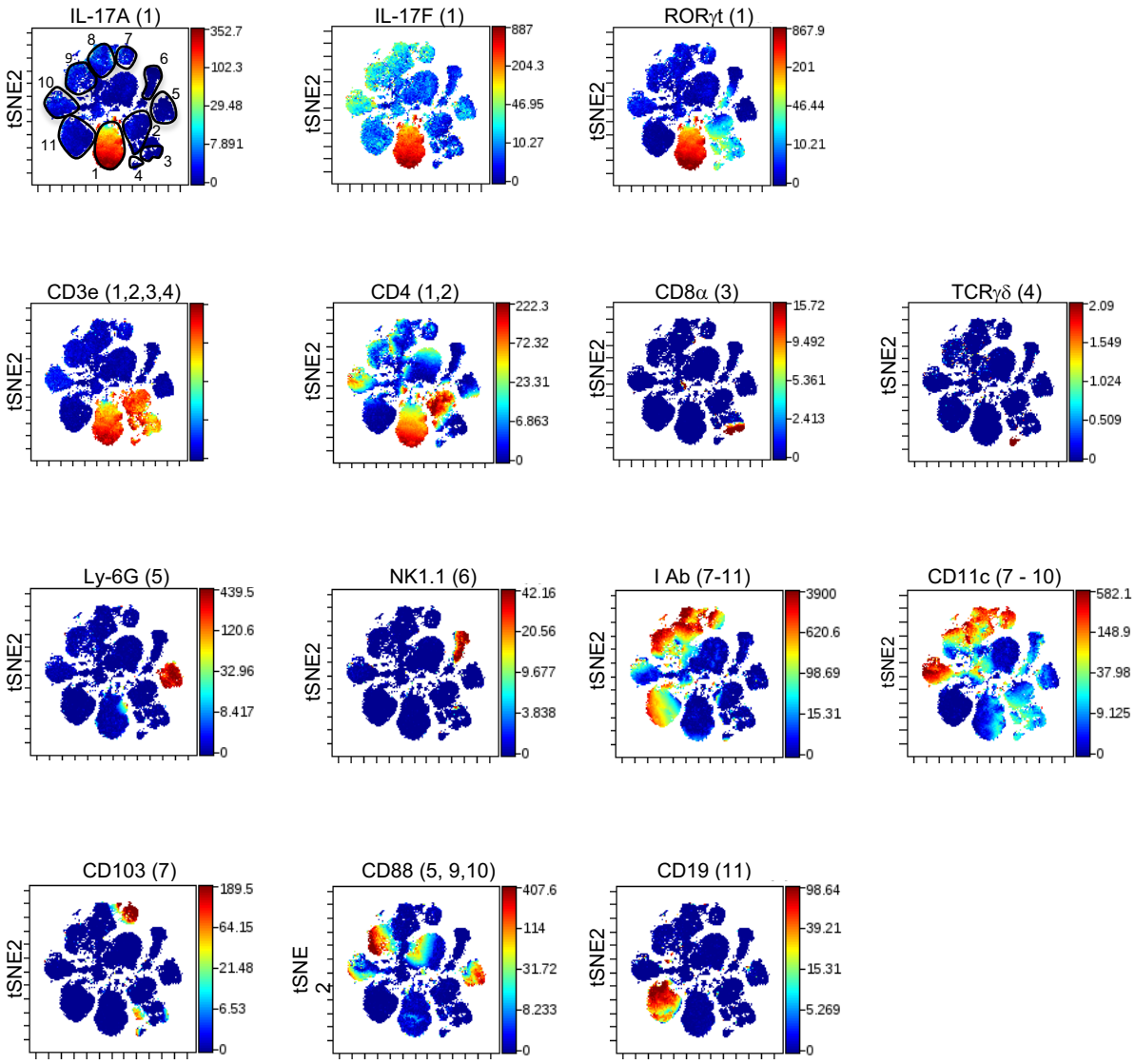

**Supplementary Figure S5**. **Confocal image of PCLS showing localization of Th17 cells**. Shown are Th17 fate mapping cells (red), IL-17 (green), IL-17-expressing Th17 cells (yellow), $CD11c^{+}$ APC's (white) and epithelial cells (blue). Images are from vehicle-treated mice (top), and VTP-treated mice (bottom). White rectangles represent areas shown at higher power in Figure 4D. Data shown are from a single experiment, representative of two.

Supplementary Figure S6



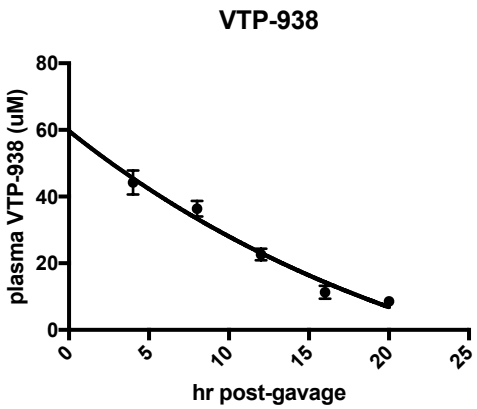

**Supplementary Figure S6**. **Effect of VTP given prior to allergen challenge on three consecutive days.** (**A**) Timeline for OVA/LPS-mediated sensitization of mice given VTP or the vehicle (veh) during the challenge phase (3 consecutive days of OVA aerosol). (**B**) Numbers of cells corresponding to the indicated leukocyte subsets in BAL at 24 h post-challenge. *N*=12 mice/group; data are combined from two experiments. Kruskal-Wallis 1-way ANOVA with Dunn's multiple comparison test. n.s.; not significant. *P<0.05, **P<0.01, ***P<0.001.

Supplementary Figure S7




**Supplementary Figure S7**. **Identification by CyTOF of cell populations in the lungs of HDE-challenged mice.** (Top) IL-17A, IL-17F and RORγt staining of cells of cell populations identified as Th17 cells (1), other CD4$^+$ T cells (2), CD8$^+$ T cells (3), TCRγδ$^+$ T cells (4), neutrophils (5), NK T cells (6), CD103$^+$ DCs (7), CD11b$^+$ DCs (8), interstitial macrophages (9), alveolar macrophages (10) and B cells (11). Also shown are staining for molecules that contribute to the identification of these cell populations.

Supplementary Figure S8




**Supplementary Figure S8**. **Plasma concentrations of VTP-938.** Mice were gavaged with 30 mg/kg VTP-938, and blood was collected at the indicated times post-gavage.

| Metal label | target | clone | Manufacturer | Catalog # |
|---|---|---|---|---|
| 141Pr | Ly-6G | 1A8 | Fluidigm | 3141008B |
| 142Nd | CD11c | N418 | Fluidigm | 3142003B |
| 143Nd | Biotin | 1D4-C5 | Fluidigm | 3143008B |
| 144Nd | FITC | FIT-22 | Fluidigm | 3144006B |
| 145Nd | PE | PE001 | Fluidigm | 3145006B |
| 148Nd | CD11b (Mac-1) | M1/70 | Fluidigm | 3148003B |
| 149Sm | CD19 | 6D5 | Fluidigm | 3149002B |
| 151Eu | CD25 (IL-2R) | 3C7 | Fluidigm | 3151007B |
| 152Sm | CD3e | 145-2C11 | Fluidigm | 3152004B |
| 153Eu | CD103 | 2E7 | Fluidigm | 3999999-1 |
| 154Sm | Siglec-F | E50-2440 | Fluidigm | 3999999-1 |
| 155Gd | CD326 (EpCAM) | G8.8 | Fluidigm | 3999999-1 |
| 156Gd | CD88 | 20/70 | Fluidigm | 3999999-1 |
| 159Tb | RORr(t) | B2D | Fluidigm | 3159019B |
| 160Gd | CD62L (L-selectin) | MEL-14 | Fluidigm | 3160008B |
| 163Dy | IL-17F | D3M4D | Harvard* | N/A |
| 165Ho | TCRgd | GL3 | Harvard* | N/A |
| 168Er | CD8a | 53-6.7 | Fluidigm | 3168003B |
| 170Er | CD161 (NK1.1) | PK136 | Fluidigm | 3170002B |
| 171Yb | CD44 | IM7 | Fluidigm | 3171003B |
| 172Yb | CD4 | RM4-5 | Fluidigm | 3172003B |
| 174Yb | IL-17A | TC11-18H10.1 | DVS Sciences | 3174002B |
| 175Lu | IAb | AF6-120.1 | Fluidigm | 3999999-1 |
| 176Yb | APC | APC003 | Fluidigm | 3176007B |
| 89Y | CD45 | 30-F11 | Fluidigm | 3089005B |
| | | | | |
| Non-metal label | target | clone | Manufacturer | |
| Biotin | CD90.2/Thy-1.2 | 53-2.1 | eBioscience | 13-0902-82 |
| APC | CD196 (CCR6) | 29-2L17 | R&D | FAB590A |
| FITC | CD31 (PECAM-1) | 390 | BD Pharmingen | 553372 |
| PE | F4/80 | BM8 | eBioscience | 12-4801-82 |

* Harvard Medical Area CyTOF Antibody Resource and Core, Boston, MA

Supplementary Table S1. List of antibodies used for CyTOF experiments.