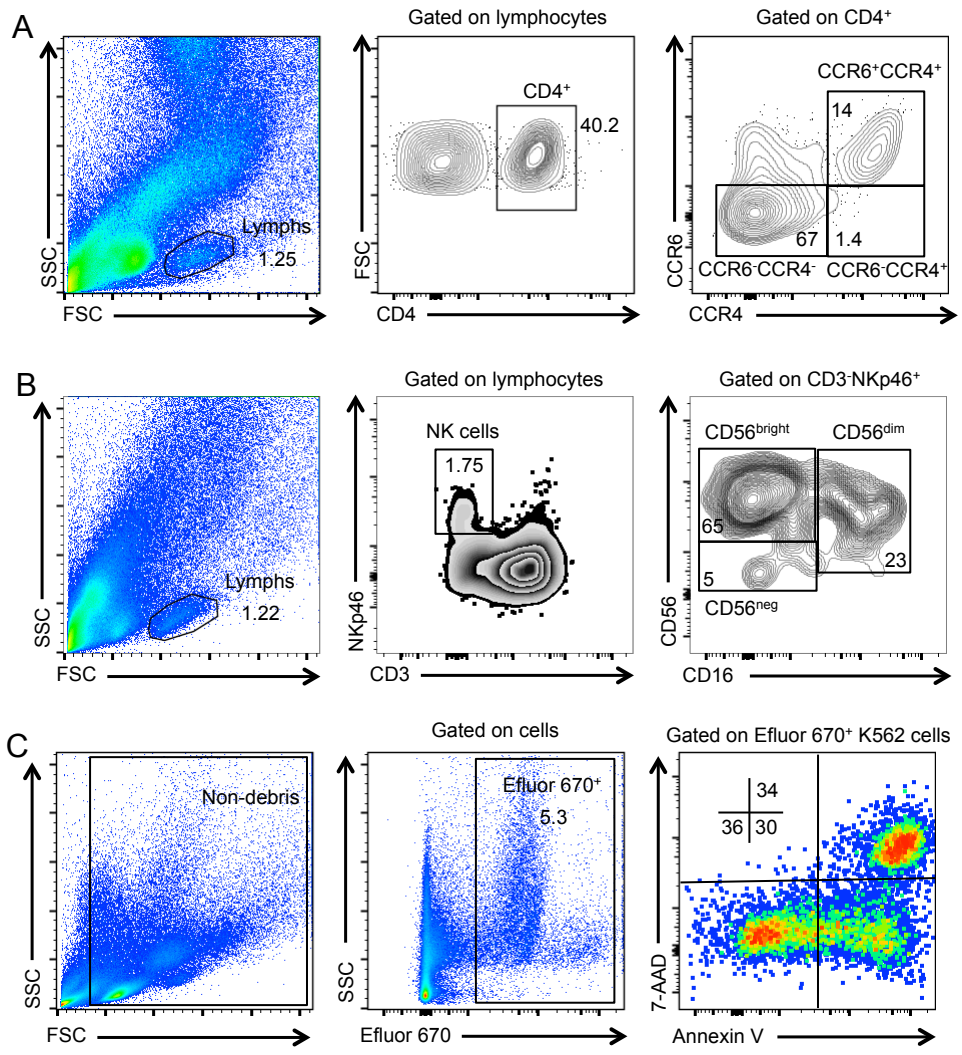

Figure S1. Flow cytometry gating strategies

(A) BAL $CD4^+$ T cells were identified as lymphocytes by FSC and SSC characteristics that expressed CD4. Surface expression of CCR6 and CCR4 was used to further define enriched helper T cells subclasses. **(B)** BAL NK cells were identified as lymphocytes by FSC and SSC characteristics that expressed NKp46 and lacked CD3 expression. Expression of CD56 and CD16 was used to further define NK cell subclasses. **(C)** PBMCs were incubated with target K562 cells (see Methods) and K562 lysis was assessed by identifying Efluor 670^+ cells and assessing Annexin V and 7-AAD staining. Numbers indicating % of targets cells in each quadrant. Representative flow cytometry plots from a severe asthma subject are shown and numbers indicate % of gated population.

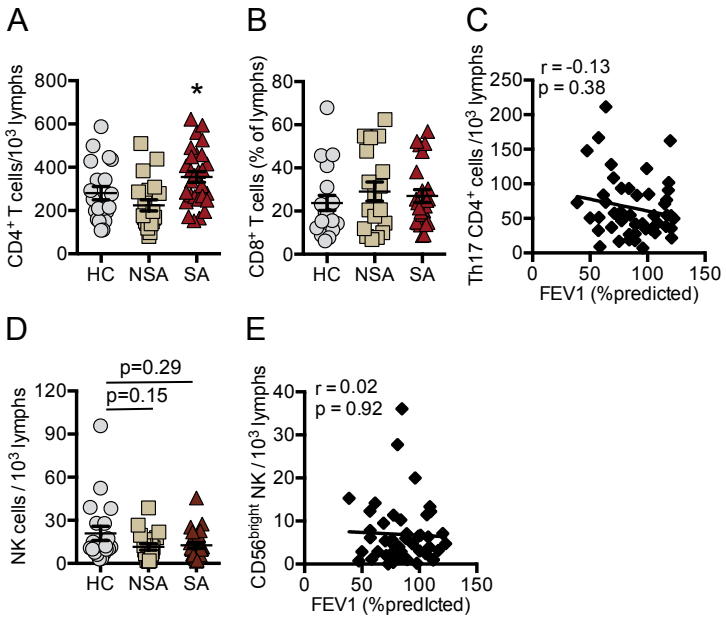

Figure S2. BAL lymphocytes in healthy and asthma subjects

BAL was obtained from healthy control (HC), non-severe asthma (NSA), and severe asthma (SA) subjects at baseline. **(A)** $CD4^+$ T cells were enumerated in BAL as number of cells per 10^3 lymphocytes. **(B)** $CD8^+$ T cells were enumerated as % of total lymphocytes**. (C)** The relationship between BAL Th17 $CD4^+$ T cells and lung function (% predicted FEV_1) was determined in asthma (diamonds) and Spearman correlation r-value and significance are noted. **(D)** NK cells were quantified as number of $CD3^-NKp46^+$ cells per 10^3 lymphocytes and **(E)** the relationship between $CD56^{bright}$ NK cells and lung function (% predicted FEV1) was determined in asthma (diamonds) and Spearman correlation r-value and significance are noted. Scatter plots show individual subject data points with overlying mean $\pm$ SEM. *$p<0.05$ compared with NSA by Kruskal-Wallis test and post hoc Dunn's multiple comparisons test.

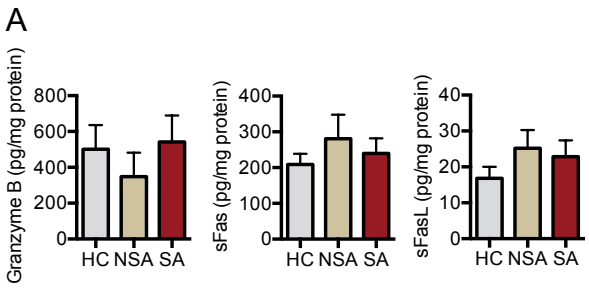

Figure S3. Levels of additional cytotoxic mediators in BALF from healthy and asthma subjects

BALF was obtained from healthy control (HC), non-severe asthma (NSA), and severe asthma (SA) subjects at baseline. **(A)** Cytotoxic mediators were measured in cell-free BALF by cytokine bead array and normalized to protein (see Methods). Values represent mean $\pm$ SEM. Analyzed by Kruskal-Wallis test.

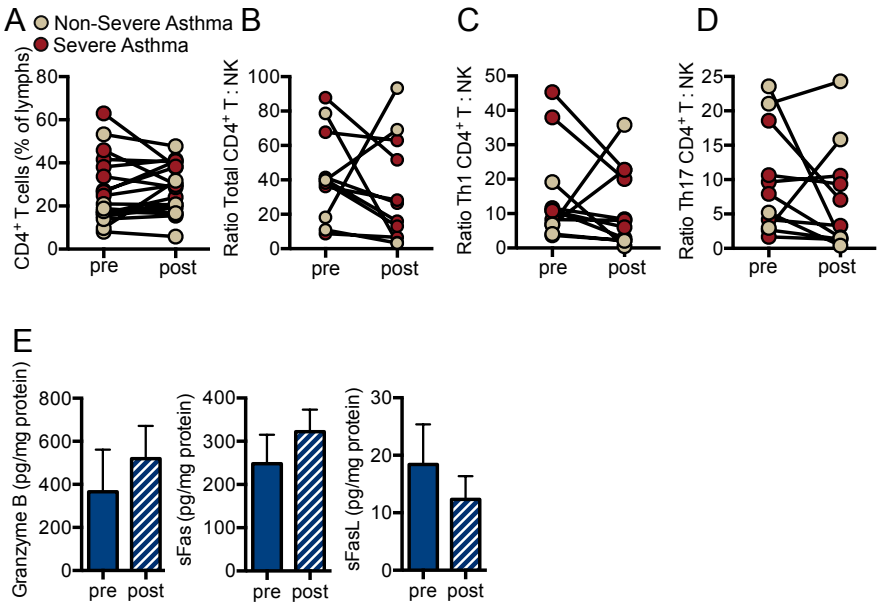

Figure S4. Systemic triamcinolone does not alter BAL CD4$^+$ T cell number or the ratio of effector CD4$^+$ T cells to NK cells in asthma

BAL was performed in asthma subjects at baseline and 3 to 6 weeks after intramuscular triamcinolone. **(A)** BAL CD4$^+$ T cell number (% of lymphocytes), **(B)** ratio total CD4$^+$ T cells: NK cells, **(C)** ratio Th1-enriched CD4$^+$ T cells: NK cells, and **(D)** ratio Th17-enriched CD4$^+$ T cells: NK cells were compared pre- and post-triamcinolone in NSA (tan) and SA (red) subjects (n=11-18 subjects). **(E)** Cytotoxic mediators were measured in cell-free BALF pre- and post-triamcinolone by cytokine bead array in n=18 asthmatic subjects. Analyzed by Wilcoxon matched-pairs signed rank test.

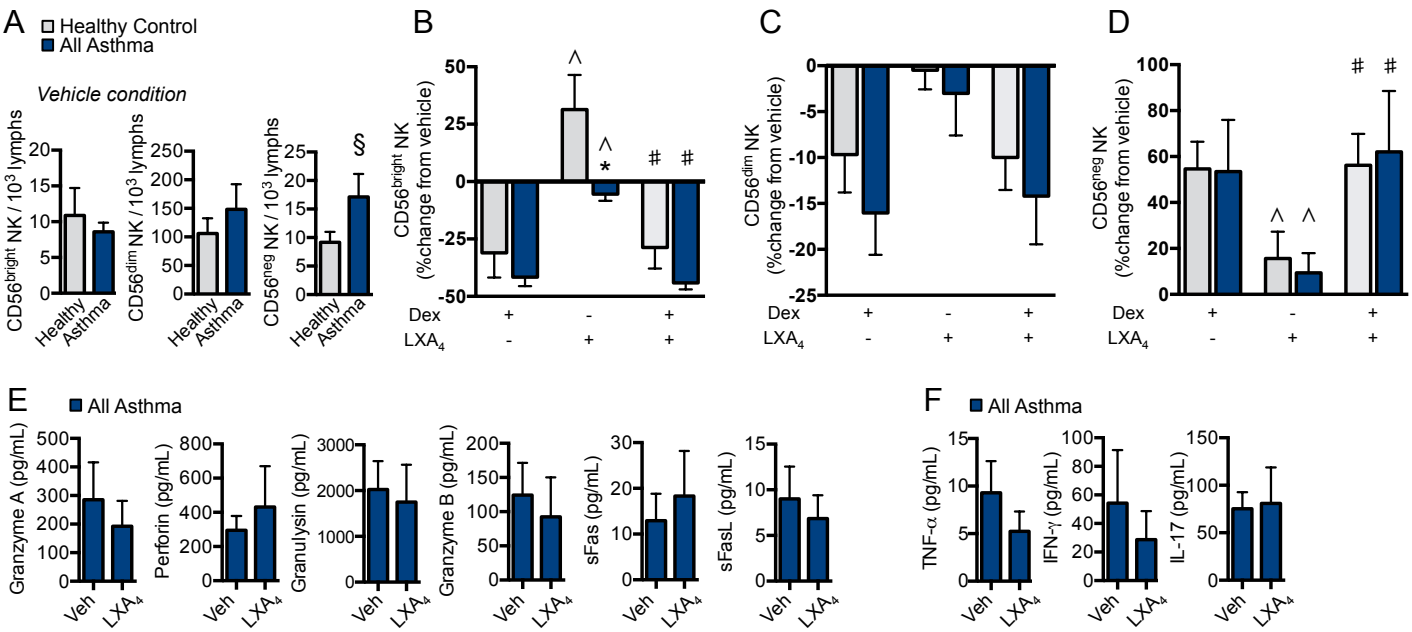

Figure S5. Exposure to dexamethasone or LXA_4 changes peripheral blood NK cell phenotype and LXA_4 exposure does not impair NK cell release of cytotoxic mediators

PBMCs from healthy donors (grey bars, n=6) or asthma subjects (blue bars, n=6) were exposed to vehicle, dexamethasone (Dex) 1μM, lipoxin A_4 (LXA_4) 50nM or Dex and LXA_4 for 48 hours. NK cells were identified by flow cytometry as $CD3^-NKp46^+$ cells with lymphoid morphology and NK cell phenotype was determined by expression of CD56 and CD16 as in Figure 2. **(A)** The numbers of each NK cell subset were determined in the vehicle condition. Changes in the numbers of **(B)** $CD56^{bright}$, **(C)** $CD56^{dim}$, and **(D)** $CD56^{neg}$ NK cells after exposure to each experimental condition for 48 hours was determined as % change relative to vehicle. **(E)** Cytotoxic mediators and **(F)** cytokines were measured in cell-free supernatant from co-culture experiments with paired comparisons made between Veh and LXA_4 conditions in n=5 asthma subjects. Values represent mean ± SEM. *$p<0.05$ and §$p<0.10$ compared with health, ^$p<0.05$ compared with Dex, and #$p<0.05$ compared with LXA_4 by ANOVA with Holm-Sidak's correction for multiple comparisons.

Supplemental Table 1. Subject number (n) for each experiment

	Healthy (n)	Non-severe Asthma (n)	Severe Asthma (n)
Figures 1 and S2			
CD4 panels	20	21	28
NK panels	20	20	25
CD8 panel	20	18	24
Ratio CD4/NK	19	19	25
Ratio PMN/NK	19	19	24
Figure 2 and S3			
NK panels	20	20	25
Mediator analysis	21	23	29
Figure 3 and S4			
Pre-post NK panels	n/a	4	7
Pre-post PMN panel	n/a	7	10
Pre-post mediator analysis	n/a	7	11
Pre-post CD4 panels	n/a	8	10
Pre-post CD4: NK ratio panels	n/a	4	7
Figure 4			
NK panels	20	20	25
CD4 panels	20	21	28
PMN panel	20	22	27