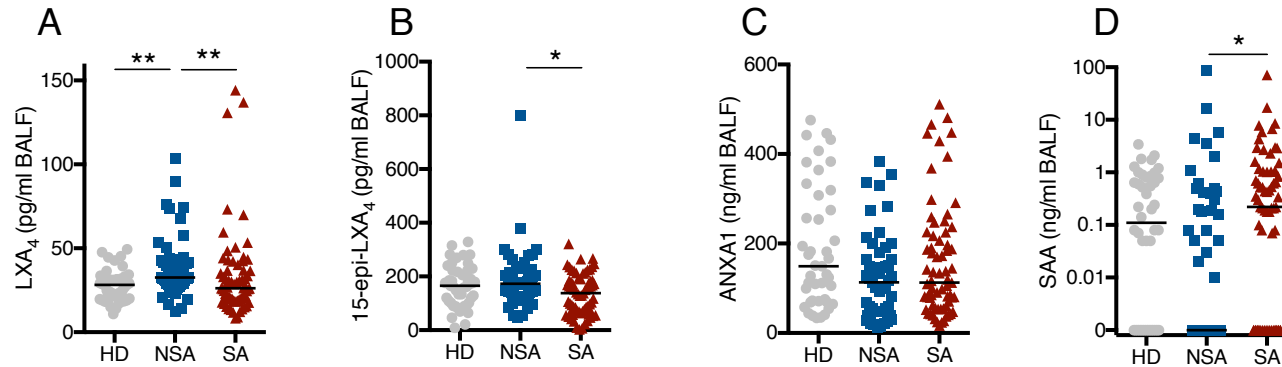


Supplemental Figure 1

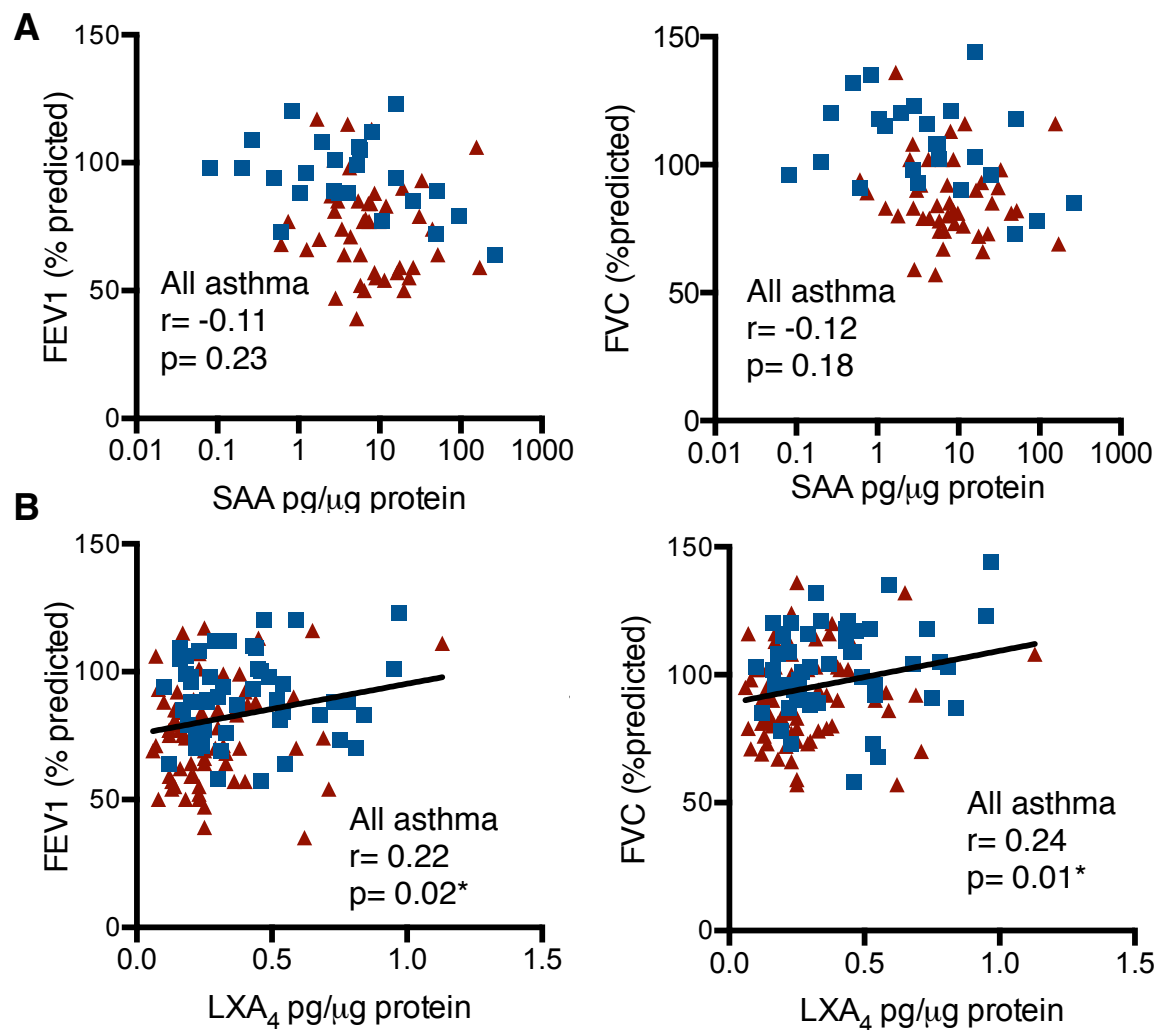


Supplemental Figure 1. Relative abundance of BALF ALX ligands differs in asthma.

BALF was obtained from subjects with asthma (n=120) and HD (n=47, grey). Asthmatic subjects were assigned to NSA (n=51, blue squares) and SA (n=69, red triangles) cohorts by SARP criteria. **(A)** LXA₄ and **(B)** 15-epi-LXA₄ were extracted from BALF and quantitated by ELISA (see Methods). **(C)** ANXA1 and **(D)** SAA levels were determined by ELISA. Scatter plots show individual data points for each subject with the median value noted by the horizontal line .

*p<0.05, **p<0.01 Kruskal-Wallis test followed by Dunn's test for multiple comparisons. BALF, bronchoalveolar lavage fluid; HD, healthy donors; NSA, non-severe asthma; SA, severe asthma; LXA₄, lipoxin A₄; 15-epi-LXA₄, 15-epimer lipoxin A₄; ELISA, enzyme-linked immunosorbent assay; ANXA1, annexin A1; SAA, serum amyloid A.

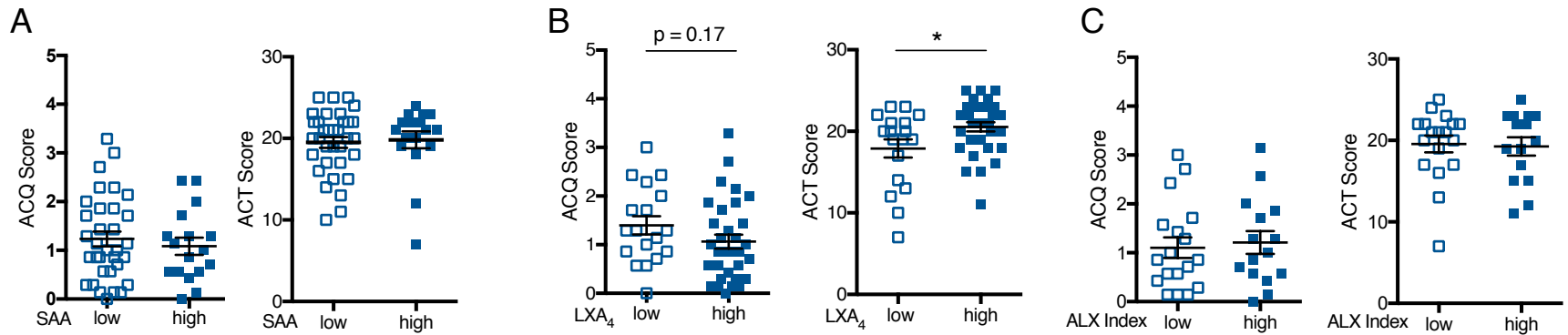
Supplemental Figure 2



Supplemental Figure 2. Relationship between lung function and BALF SAA and LXA₄ levels

BALF was obtained from subjects with asthma (n=51 NSA, blue squares; n=69 SA, red triangles) and SAA and LXA₄ levels were measured. The relationship between lung function (FEV1 and FVC (% predicted)) and **(A)** BALF SAA levels and **(B)** LXA₄ levels was determined. Pearson correlation r and p -values are noted (inset) and regression lines are shown when significant. BALF, bronchoalveolar lavage fluid; NSA, non-severe asthma; SA, severe asthma; LXA₄, lipoxin A₄; SAA, serum amyloid A. FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity.

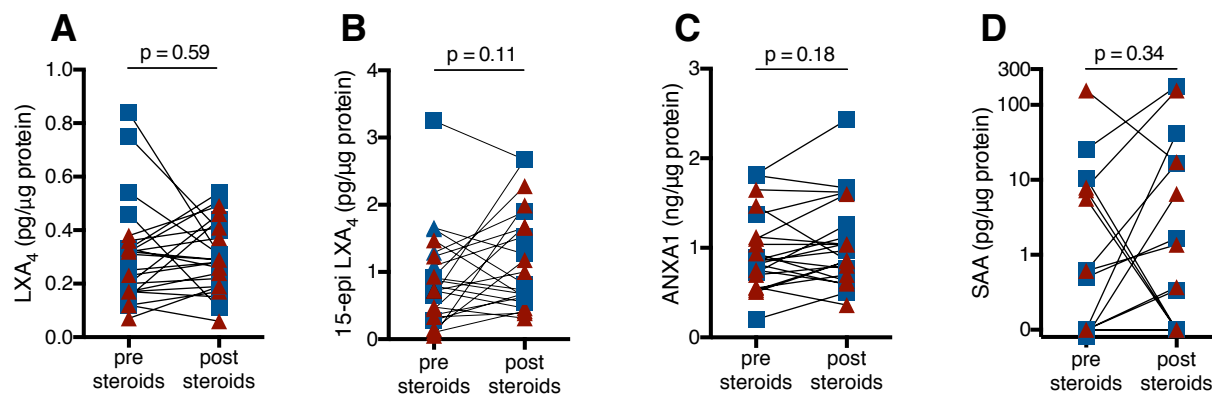
Supplemental Figure 3



Supplemental Figure 3. Relationship for asthma symptom control to ALX ligands and ALX expression in NSA.

NSA subjects were categorized into subgroups based on “low” (open squares) or “high” (closed squares) levels of SAA **(A)**, LXA₄ **(B)**, and macrophage ALX expression **(C)** using the median value for the all asthma BALF level of each variable as the cutoff between the groups. ACQ and ACT scores were compared between low and high subgroups. * $p < 0.05$ by Student’s *t*-test. ACQ, asthma control questionnaire; ACT, asthma control test; SAA, serum amyloid A; LXA₄, lipoxin A₄; ALX, airway lipoxin A₄ receptor.

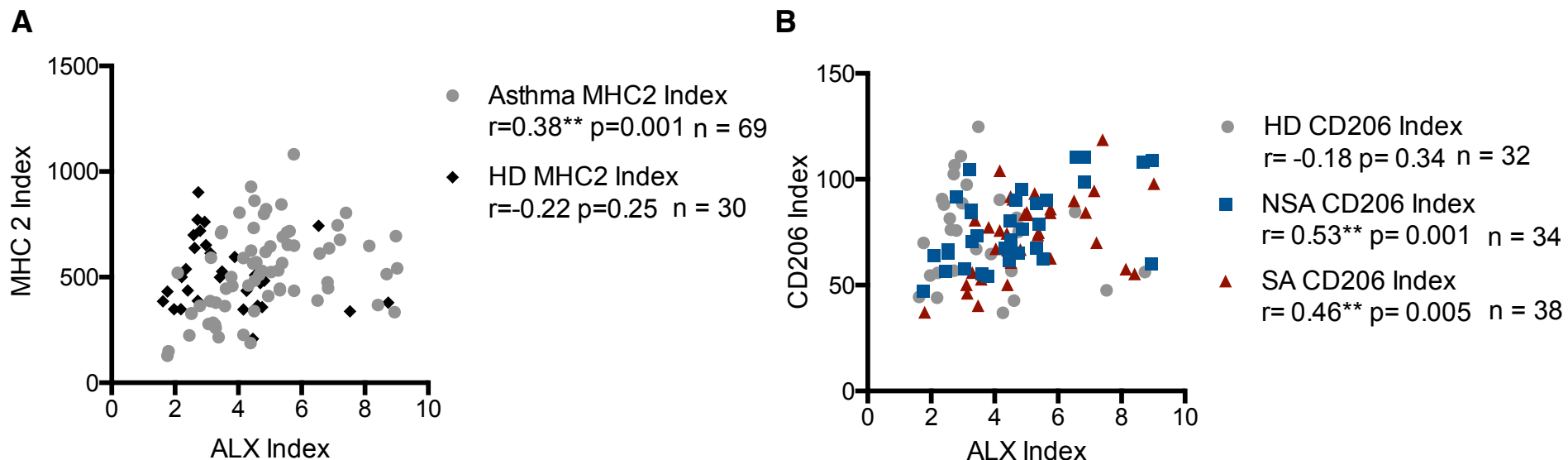
Supplemental Figure 4



Supplemental Figure 4. Influence of systemic steroid administration on BALF ALX ligands.

BAL was performed in asthmatic subjects at baseline and 3 to 6 weeks after intramuscular triamcinolone. BALF levels of (A) LXA₄, (B) 15-epi-LXA₄, (C) ANXA1 and (D) SAA were measured by ELISA before and after triamcinolone in n=10 NSA (blue) and n=12 SA (red) and normalized to BALF protein levels. Wilcoxon matched-paired signed rank test was used to assess differences in levels before and after triamcinolone. LXA₄, Lipoxin A₄; 15-epi-LXA₄, 15-epimer lipoxin A₄; ANXA1, annexin A1; SAA, serum amyloid A; HD, healthy donors; NSA, non-severe asthma; SA, severe asthma; ELISA, enzyme-linked immunosorbent assay; BALF, bronchoalveolar lavage fluid.

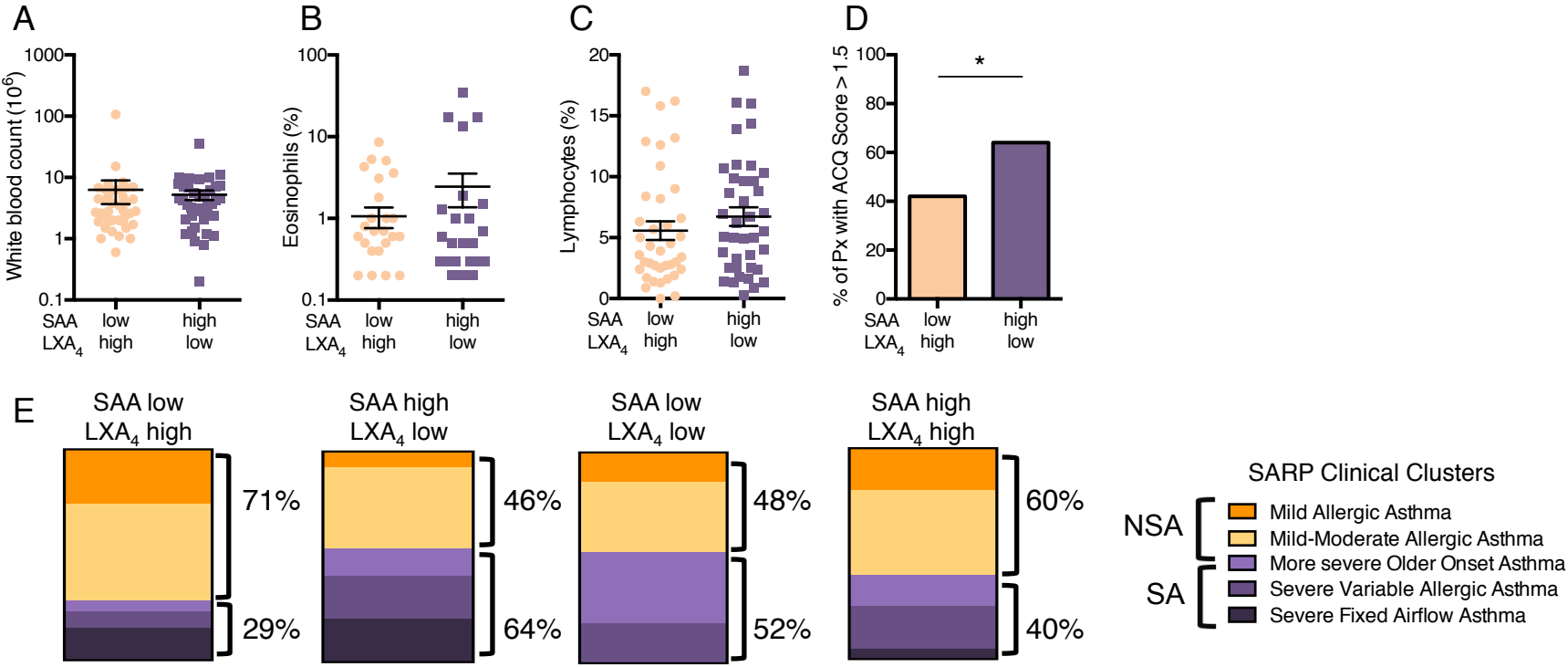
Supplemental Figure 5



Supplemental Figure 5. ALX expression on BAL macrophages correlates with MHC2 and CD206 expression in asthma.

BAL cellular samples were obtained and flow cytometry analysis of macrophages was performed. Macrophages were identified as single, live, CD206⁺ cells and the MFI Index of ALX, MHC II and CD206 were determined. MFI index is defined as the MFI of the antigen divided by the MFI of the isotype control. The relationship between the ALX index and **(A)** the MHC2 index or **(B)** the CD206 index was determined by Pearson's correlation analysis. Noted in each graph are the Pearson correlation r and p -values for each cohort tested. MHC2, major histocompatibility class 2; ALX, airway lipoxin A₄ receptor; HD, healthy donors; NSA, non-severe asthma; SA, severe asthma

Supplemental Figure 6



Supplemental Figure 6. BAL leukocytes and symptom control for asthma patients with endogenous SAA^{low}LXA₄^{high} and SAA^{high}LXA₄^{low} levels.

(A) BALF total white blood cell count, **(B)** % eosinophils and **(C)** % lymphocytes were determined for LXA₄^{high}SAA^{low}(beige) and LXA₄^{low}SAA^{high}(purple) asthma subjects. **(D)** The percentage of asthma subjects with an ACQ score > 1.5 was compared between subjects with endogenous LXA₄^{high}SAA^{low} (beige) and LXA₄^{low}SAA^{high} (purple). *p<0.05 by chi-squared test. **(E)** Subjects in each of the four LXA₄ SAA subgroups were assigned to clinical clusters as defined in SARP-1 (5) and the percent of subjects assigned to NSA clusters and SA clusters is indicated for each subgroup. LXA₄, lipoxin A₄; SAA, serum amyloid A.

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