Table E1. Correlations between Biomarkers Overall and by BMI Group.

Group	Marker	IL-6	TNF-α	FVC (%)	FEV_1 (%)
Overall	**SP-A**	-0.19 (-0.48, 0.13)	-0.06 (-0.37, 0.26)	0.21 (-0.06, 0.45)	0.17 (-0.10, 0.42)
	IL-6		**0.82* (0.67, 0.90)**	-0.22 (-0.50, 0.10)	-0.002 (-0.32, 0.31)
	TNF-α			-0.27 (-0.54, 0.04)	0.06 (-0.26, 0.37)
	FVC (%)				**0.61* (0.41, 0.75)**
Lean	**SP-A**	-0.38 (-0.75, 0.16)	-0.19 (-0.64, 0.35)	0.14 (-0.29, 0.52)	0.12 (-0.31, 0.51)
	IL-6		**0.90* (0.72, 0.97**)	-0.24 (-0.67, 0.31)	0.04 (-0.48, 0.54)
	TNF-α			-0.23 (-0.67, 0.32)	0.17 (-0.38, 0.63)
	FVC (%)				**0.47* (0.07, 0.74)**
Over-weight	**SP-A**	-0.31 (-0.83, 0.50)	-0.47 (-0.88, 0.35)	-0.17 (-0.45, 0.68)	-0.03 (-0.59, 0.55)
	IL-6		**0.82* (0.26, 0.97)**	-0.28 (-0.82, 0.53)	-0.13 (-0.76, 0.63)
	TNF-α			-0.15 (-0.77, 0.62)	0.09 (-0.66, 0.75)
	FVC (%)				**0.72* (0.25, 0.92)**
Obese	**SP-A**	0.12 (-0.40, 0.58)	0.23 (-0.30, 0.65)	0.21 (-0.26, 0.60)	0.16 (-0.31, 0.56)
	IL-6		**0.82* (0.55, 0.94)**	-0.17 (-0.61, 0.35)	0.04 (-0.47, 0.52)
	TNF-α			-0.27 (-0.67, 0.26)	0.07 (-0.44, 0.55)
	FVC (%)				**0.70* (0.38, 0.87)**

*Denotes a statistically significant correlation. Data presented as the Pearson correlation coefficient with 95% confidence intervals.

Table E2. Univariable and multivariable regression models predicting Biomarkers by BMI,

Model	Variable	Univariable			Multivariable (Full)			Multivariable (Reduced)		
		PE ± SD	P-value	R^2	PE ± SD	P-value	R^2	PE ± SD	P-value	R^2
SP-A	BMI	-0.05 ± 0.02	0.014	0.109	-0.02 ± 0.03	0.646	0.134			0.130
	Asthma	-0.08 ± 0.28	0.775	0.002	1.35 ± 1.14	0.243		1.76 ± 0.72	0.017	
	BMI by Asthma				-0.05 ± 0.04	0.229		-0.06 ± 0.02	0.008	
FEV_1 (%)	BMI	-0.41 ± 0.26	0.119	0.045	-0.25 ± 0.43	0.560	0.163			0.133
	Asthma	-10.13 ± 3.55	0.006	0.133	-6.26 ± 15.07	0.680		-10.13 ± 3.55	0.006	
	BMI by Asthma				-0.11 ± 0.53	0.823				
FVC (%)	BMI	-0.51 ± 0.26	0.056	0.067	0.10 ± 0.45	0.823	0.125			0.124
	Asthma	1.46 ± 3.90	0.709	0.003	28.79 ± 15.79	0.074		26.03 ± 9.88	0.011	
	BMI by Asthma				-0.95 ± 0.55	0.091		-0.85 ± 0.32	0.010	
TNF-α	BMI	0.02 ± 0.14	0.902	0.000	0.27 ± 0.26	0.823	0.071			
	Asthma	-2.64 ± 2.10	0.218	0.041	6.11 ± 8.91	0.074				
	BMI by Asthma				-0.31 ± 0.31	0.313				
IL-6	BMI	-0.03 ± 0.15	0.828	0.001	0.03 ± 0.28	0.923	0.024			
	Asthma	-2.10 ± 2.26	0.359	0.023	-0.41 ± 9.72	0.966				
	BMI by Asthma				-0.06 ± 0.33	0.862				

***Bronchoscopy and bronchoalveolar lavage (BAL) were performed and SP-A, TNF-□ and IL-6 were quantified in our study subjects*.** BAL samples were centrifuged at 10,000 rpm for 20 minutes. The pelleted samples were examined by Western blot analysis for the presence of SP-A (Abcam, ab51891). The levels of SP-A per sample were determined by densitometry for SP-A as a fraction of the total protein of each sample (determined by BCA analysis). SP-A levels were also detected in a subset of pelleted BAL samples by ELISA (Biovendor; Cat# RD191139200R); in the same subset of pelleted BAL samples, TNF-α and IL-6 were quantitated by multiplex Luminex analysis (Millipore).

OVA and HDM models. For the OVA model, SP-$A^{-/-}$ mice were sensitized via intraperitoneal (i.p.) injections of 30 μg of OVA (Sigma) emulsified in Aluminum Hydroxide gel (Sigma) on days 1 and 14 and challenged with 1% OVA aerosol on days 21–23 via nebulizer. Approximately 24 hours after the last OVA aerosol, SP-A was given via intratracheal (*i.t.*) administration at a dosage of 25 μg per mouse in 50 μl of sterile saline. For the HDM model, SP-$A^{-/-}$ mice were given 100 μg HDM extract (prepared from total dry weight; Greer) in a volume of 50 μl via intranasal administration on days 0, 7 and 14. Approximately 24 hours after the last HDM dose, SP-A was given via intratracheal (*i.t.*) administration at a dosage of 25 μg per mouse in 50 μl of sterile saline. For both the OVA and HDM models, after an additional 6 days, mice were euthanized and lung tissue was stained with anti-MBP and analyzed for the presence of tissue eosinophils by a trained lung histopathologist.

Histological analysis of tissue eosinophilia with anti-MBP. In brief, antigen-retrieval was carried out by incubating in 0.1% trypsin in PBS and 0.1% $CaCl_2$ (pH 7.8) for 30 min at 90^{o}C. After washing with 0.05% Tween 20 in PBS with 1% bovine serum albumin (PBS/BSA) (Sigma), lung sections were blocked with 10% normal goat serum in PBS (Vector Laboratories, Burlingame, CA) and

then incubated with 1:500 dilution of rabbit anti-mouse MBP in 1% BSA overnight at 4^{o}C in a humid chamber.

RT-PCR primers: Murine SP-A (forward 5' GTA CAG TAG CCA TGT CAC TAG G 3', reverse 5' TGA AGC TCC TCA TCC AGG TAA G 3') and Cyclophilin (forward 5' AGC ACT GGA GAG AAA GGA TTT GG 3', reverse 5' TCT TCT TGC TGG TCT TGC CAT T 3').

Statistical Analysis*:* Descriptive statistics were computed including the mean and standard deviation or median and range for continuous variables as determined by the data distribution, while counts and percentages were used to describe categorical variables with non-missing values. Normality was assessed by using the Kolmogorov-Smirnov test and by reviewing normality plots. Body mass index (BMI) was treated as both a continuous and a categorical variable with three categories: lean (BMI < 25), overweight (25 ≤ BMI < 30), and obese (BMI ≥ 30). Six groups based on categorical BMI and asthma status were created, including lean normal (LN), lean asthma (LA), overweight normal (OWN), overweight asthma (OWA), obese normal (ON) and obese asthma (OA). Pairwise comparison of interest was between obese asthma (OA) and all other BMI/asthma groups combined (Control).

An analysis of variance (F-test) or Kruskal-Wallis test was used to make comparisons between obese asthma and the control group for continuous variables based on the distribution, while the chi-square test or Fisher's exact test (expected cell counts < 5) was used for categorical variables. Pearson's correlation coefficients with 95% confidence intervals (based on Fisher's Z transformation) were used to determine the relationship among SP-A, FEV_1 (% predicted), FVC (% predicted), TNF-α, and IL-6

overall and within each weight category. Linear regression models were used to determine both the univariable and multivariable correlation for each of SP-A, FEV_1 (% predicted), FVC (% predicted), TNF-α, and IL-6 with continuous BMI, asthma status and the interaction between BMI and asthma.

In murine experiments, the Kruskal-Wallis test and chi-square test were used to make comparisons on the basis of obesity and/or experimental condition. Linear regression was again used to determine the correlation between BMI and SP-A levels in murine BAL. The t-test was used to determine statistically significant differences in the murine models.

Analyses were performed using SAS© version 9.4 and SAS JMP© (SAS Institute, Inc., Cary, NC) and Graph Pad Prism. We did not adjust for multiple comparisons as all analyses were exploratory, and pairwise comparisons were avoided as much as possible by evaluating linear trends or differences across pre-specified groups and by presenting confidence intervals. Statistical significance was defined as a p-value ≤ 0.05.