

Type 1 immunity predominates in Chronic Bronchitis patients with COPD in UCLA-AMGEN COPD Phenotyping cohort

Sydney Silverman¹⁾, Igor Barjaktarevic¹⁾

¹Division of Pulmonary and Critical Care Medicine, David Geffen School of Medicine, University of California Los Angeles

Rationale – Immunophenotyping in COPD

- Immunophenotyping: quantifying immune system components → helping to define inflammatory mechanisms and therapeutic targets in COPD
- Inflammation can be broadly classified into **Type 1, Type 2, and Type 3** pathways
- Importantly, inflammatory pathways may vary in their response to different therapies

	TYPE 1 (Th1)	TYPE 2 (Th2)	TYPE 3 (Th17)
Primary immune cells	Th1 , NK, macrophages	Th2 , eosinophils, mast cells, basophils	Th17 , neutrophils
Key cytokines	IFN- γ , TNF- α , IL-12, IL-18	IL-4, IL-5, IL-13	IL-17A, IL-17F, IL-22, IL-23
Major functions	Intracellular pathogen defense, macrophage activation	Eosinophilic/allergic inflammation, mucus production, helminth/parasite defense	Defense against extracellular bacteria/fungi
Potential airway relevance	Interferon-driven, macrophage-predominant inflammation	Type 2 / eosinophilic airway inflammation	Neutrophilic inflammation

Focus & Knowledge Gap

- **Chronic bronchitis (CB)** is a common COPD phenotype characterized by chronic mucus hypersecretion and airway inflammation, and is associated with worse clinical outcomes.

What has been studied:

- Blood/sputum cytokine profiles
- Innate immune cells
 - Neutrophils, macrophages, eosinophils
- Changes during exacerbations vs stable disease

What is missing:

- Adaptive immune profiling specifically in stable CB
 - T-helper subset distributions Th1, Th2, Th17 (CD4+ T-cell differentiators)

Objective

- **Gap/Focus:** It is unclear whether CB reflects a distinct adaptive immune endotype in stable COPD

Objective: To characterize immune profiles in CB vs non-CB COPD, hypothesizing that a Type 1 immune response predominates over Type 2 immune responses in patients with clinically stable COPD with CB.

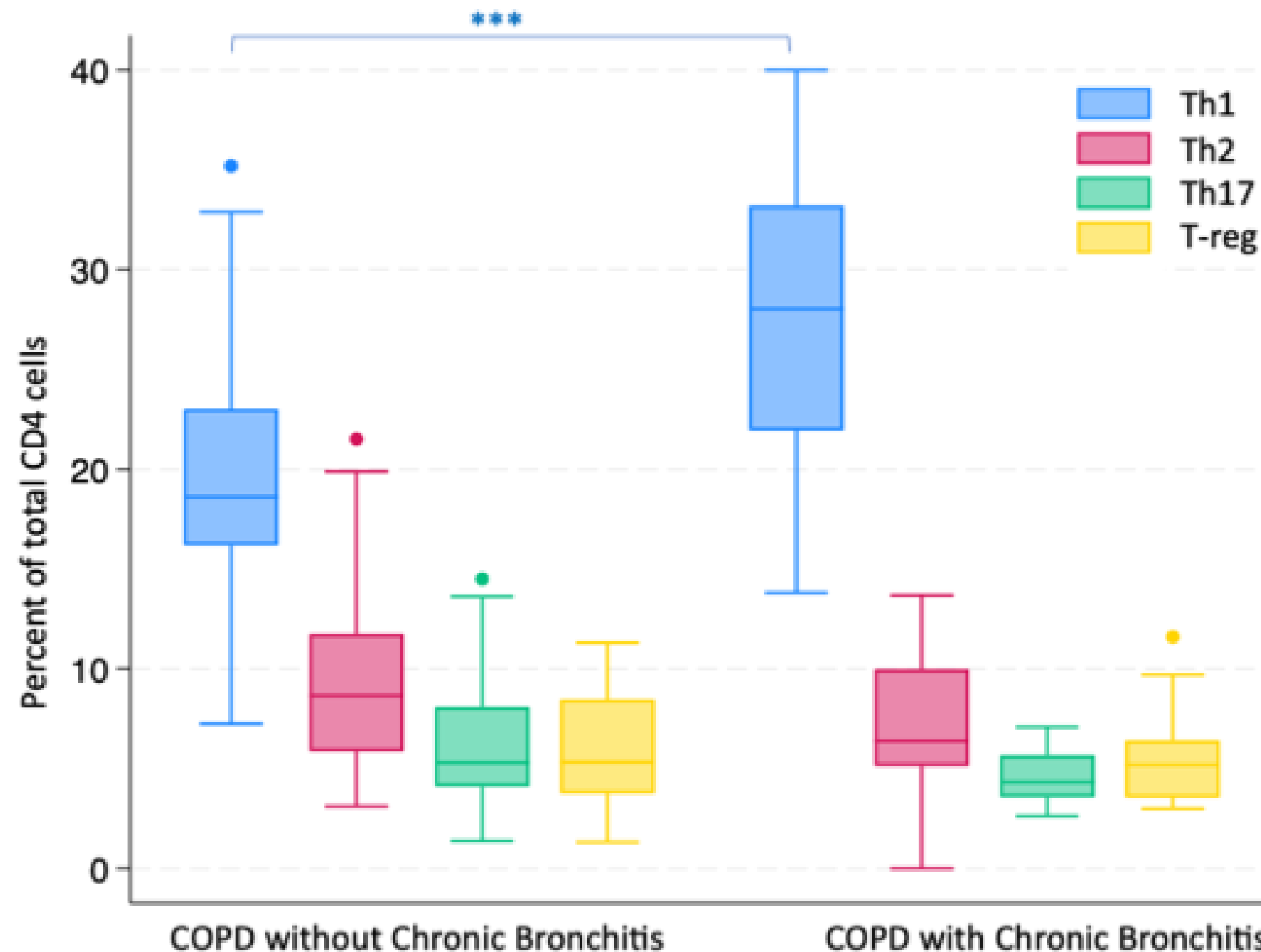
- Prospective single-center COPD cohort
 - Stable COPD, age 40–80
 - Post-BD $FEV_1/FVC < 0.70$
 - ≥ 10 pack-year smoking history
 - Between-group comparison: Kruskal–Wallis rank-sum test + Fisher's exact test
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Stable COPD Cohort, N = 82

- Age: 70 ± 7 years
- Gender: 40% female
- Smoking history: 47 pack-years
- Spirometry: Moderate airflow obstruction, FEV_1 : $61 \pm 24\%$ predicted
- Chronic bronchitis (defined by MRC criteria) prevalence
 - CB: n = 19; (23%)
 - Non-CB: n = 63

Results

CB is associated with increased Th1 cells



**%Th1 ↑ in CB (28.1 (22.0, 33.2)% vs. 18.6 (16.2, 23.0)%,
P = 0.006)**

No major change in

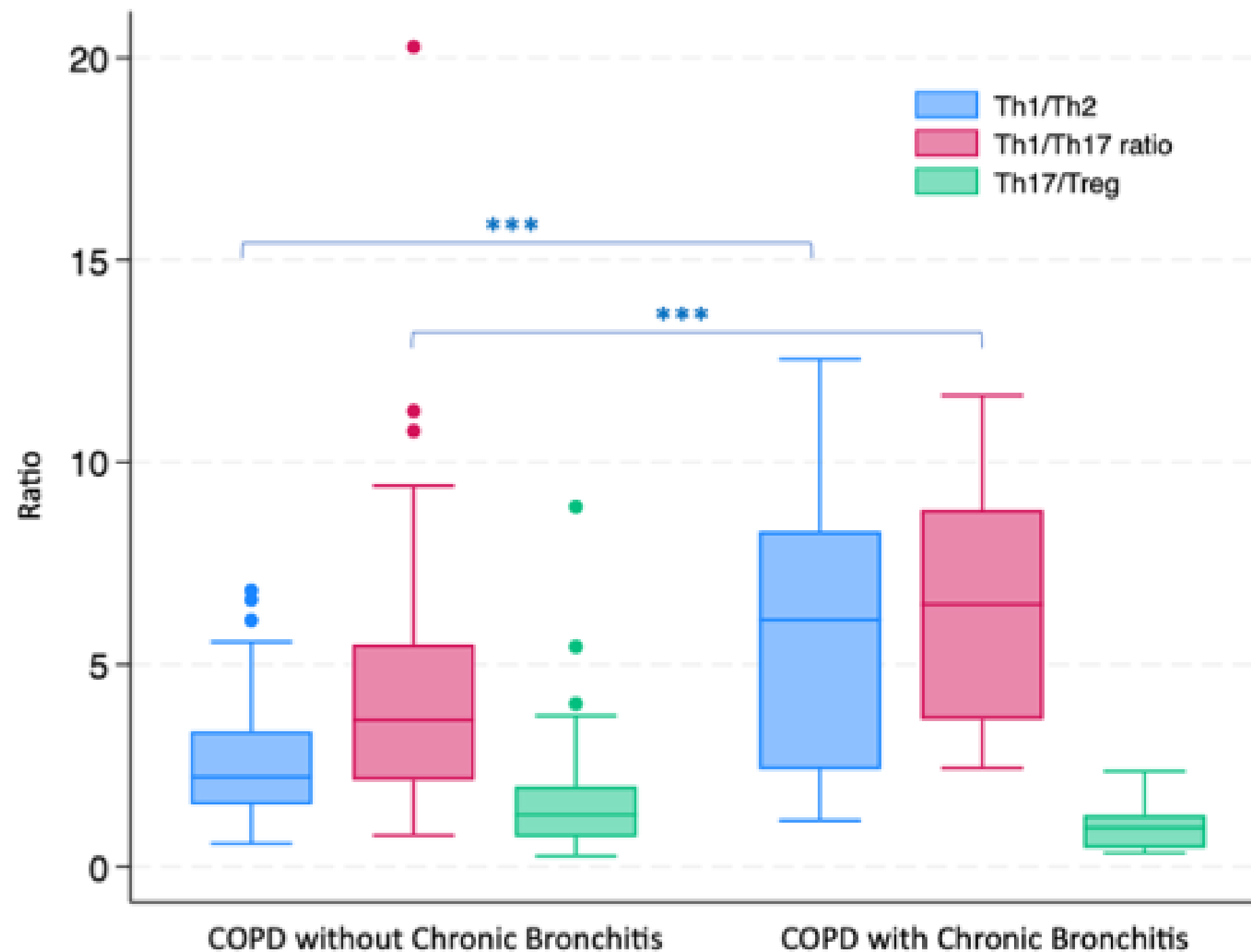
- WBC, total T cells, CD4/CD8
- Th2, Th17, Treg

(Determined via Kruskal-Wallis rank sum test)

Demonstrated Type 1-skew in CB rather than a broad shift across all Th subsets.

Results

CB is associated with an increased Th1/Th2 and Th1/Th17 ratio



Th1/Th2 ratio ↑ (P = 0.005)
Th1/Th17 ratio ↑ (P = 0.009)

Multivariable logistic regression:

- An increased Th1/Th2 ratio was independently associated with higher odds of CB (OR 1.49, 95% CI 1.01–2.31, P = 0.046)

Adjustment for age, sex, race, smoking status, pack years, ESR, and FEV₁

CB showed association not just with higher Th1 cells, but with a broader Type 1–predominant immune balance.

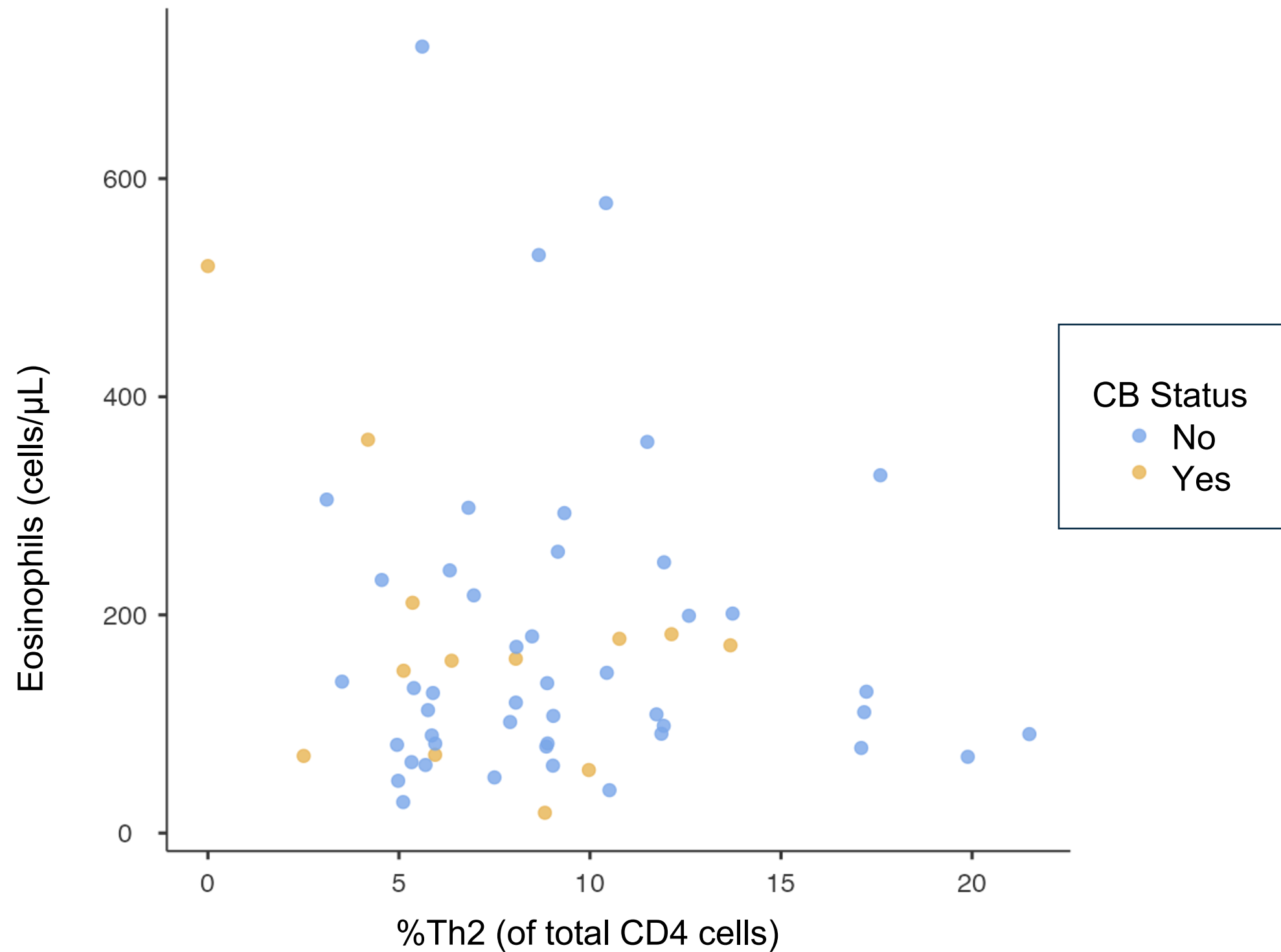
Type 1-shift in CB without an eosinophil/Type 2 shift

1. No difference in eosinophil cell counts or percentages between CB and non-CB groups.
2. Clinically stable patients with elevated blood eosinophil counts (≥ 300 cells/ μ L) comparably represented in both CB and non-CB.

Variable	Overall (n = 82)	CB (n = 19)	Non-CB (n = 63)	P-value
Blood Eos > 300 cells/ μ L	14 (17%)	3 (16%)	11 (17%)	>0.999
Eosinophils (cells/ μ L)	138.8 (82.1, 211.1)	159.8 (88.8, 211.1)	131.3 (82.0, 217.9)	0.469
Eosinophils (% WB)	2.2 (1.4, 3.3)	2.4 (1.7, 4.0)	2.1 (1.4, 3.3)	0.448
Eosinophils (% Sputum)	0.1 (0.0, 0.6)	0.4 (0.0, 1.6)	0.0 (0.0, 0.6)	0.239

Results

No observed relationship between Th2 cells and eosinophils in our cohort



No significant correlation between Th2 cells and blood eosinophil counts

Spearman's rank correlation:

- Non-CB: $\rho = 0.072$, $P = 0.632$
- CB: $\rho = -0.181$, $P = 0.554$
- Whole cohort: $\rho = 0.008$, $P = 0.954$

Eosinophils did not appear to track with adaptive Type 2 immune activity in peripheral blood

CB may reflect a Type 1-skewed endotype

- Chronic bronchitis was associated with a Type 1-skewed adaptive immune profile in our cohort
 - Signal driven by higher Th1 cells and Th1/Th2 balance without a relative attenuation of Type 2, or eosinophilic inflammation
 - Reinforces prior literature emphasizing neutrophilia and increased TNF- α in CB
- Supports CB as a biologically distinct inflammatory phenotype within COPD
- Dissociation between eosinophils and Th2 signatures in our cohort
- Supports the development and further research of endotype-driven treatment strategies

THANK YOU



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**David Geffen
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Extra materials

Table 1
Demographics and clinical characteristics of study participants with stable COPD

Variable	Overall (n = 82 ¹)	CB (n = 19 ¹)	Non-CB (n = 63 ¹)	P-value ²
Age (years)	70.1 ± 7.1	69.6 ± 5.4	70.2 ± 7.5	0.324
Female	33 (40%)	9 (47%)	24 (38%)	0.595
Race				0.390
White	53 (65%)	10 (53%)	43 (68%)	
Black or African American	23 (28%)	7 (37%)	16 (25%)	
Asian	4 (4.9%)	1 (5.3%)	3 (4.8%)	
Other	2 (2.4%)	1 (5.3%)	1 (1.6%)	
BMI (kg/m2)	27.2 ± 5.0	27.2 ± 5.5	27.2 ± 4.9	0.921
Smoking pack years	46.9 ± 31.1	42.5 ± 26.8	48.2 ± 32.4	0.540
Current smoker	17 (21%)	5 (26%)	12 (19%)	0.526
FVC (% predicted)	94.4 ± 51.4	114.5 ± 96.2	88.3 ± 24.5	0.574
FEV1 (% predicted)	61.2 ± 23.9	57.3 ± 21.1	62.3 ± 24.8	0.396
FEV1/FVC	66.5 ± 18.2	58.1 ± 19.0	69.0 ± 17.3	0.044*
GOLD Group				0.076
A	24 (30%)	2 (11%)	22 (35%)	
B	40 (49%)	11 (58%)	29 (47%)	
E	17 (21%)	6 (32%)	11 (18%)	
Home O2	7 (9.9%)	3 (17%)	4 (7.5%)	0.359
CAT	14.7 ± 8.9	21.6 ± 9.3	12.6 ± 7.8	<0.001***
mMRC,				0.115
0	23 (28%)	2 (11%)	21 (34%)	
1	31 (38%)	7 (37%)	24 (39%)	
2	16 (20%)	5 (26%)	11 (18%)	
3	9 (11%)	4 (21%)	5 (8.1%)	
4	2 (2.5%)	1 (5.3%)	1 (1.6%)	
SGRQ	35.0 ± 23.6	53.0 ± 24.3	29.5 ± 20.5	<0.001***
Exacerbations	19 (30%)	6 (43%)	13 (27%)	0.324
Asthma history	25 (30%)	6 (32%)	19 (30%)	>0.999
Emphysema	9 (13%)	2 (11%)	7 (13%)	>0.999
Cardiovascular disease	49 (60%)	12 (63%)	37 (59%)	0.795
LABA	4 (6.8%)	1 (7.7%)	3 (6.5%)	>0.999
LAMA	26 (42%)	10 (71%)	16 (33%)	0.015*
ICS	6 (10%)	0 (0%)	6 (13%)	0.333
Blood Eos > 300 cells/μL	14 (17%)	3 (16%)	11 (17%)	>0.999
Fibrinogen (mg/dL)	352.4 ± 83.3	373.8 ± 109.3	345.8 ± 73.2	0.603

¹Mean ± SD; n (%)
²Kruskal-Wallis rank sum test;
Fisher's exact test

Extra materials

Table 2
Fluorescence-Activated Cell Sorting (FACS) and Serum Cytokine Analysis

Variable	Overall (n = 82 ¹)	CB (n = 19 ¹)	Non-CB (n = 63 ²)	P-value ²
CRP (mg/dL)	0.3 (0.3, 0.6)	0.4 (0.3, 1.1)	0.3 (0.3, 0.5)	0.115
ESR (mm/h)	18.0 (10.0, 33.0)	25.0 (11.0, 37.0)	18.0 (10.0, 30.0)	0.255
Neutrophil-to-lymphocyte ratio	3.1 (2.1, 4.1)	2.7 (1.7, 4.0)	3.1 (2.2, 4.2)	0.429
WBC ($\times 10^9$ / μ L)	6.9 (5.6, 7.7)	7.1 (6.4, 7.4)	6.8 (5.4, 8.1)	0.524
PMN (% WB)	68.0 (60.8, 71.6)	63.3 (56.3, 68.7)	68.7 (64.2, 72.2)	0.224
Eosinophils (cells/ μ L)	138.8 (82.1, 211.1)	159.8 (88.8, 211.1)	131.3 (82.0, 217.9)	0.469
Eosinophils (% WB)	2.2 (1.4, 3.3)	2.4 (1.7, 4.0)	2.1 (1.4, 3.3)	0.448
Eosinophils (% Sputum)	0.1 (0.0, 0.6)	0.4 (0.0, 1.6)	0.0 (0.0, 0.6)	0.239
Neutrophils (% WB)	65.9 (57.4, 71.1)	64.4 (54.0, 71.5)	66.4 (61.0, 71.1)	0.413
Neutrophils (% Sputum)	41.3 (7.3, 74.0)	35.0 (3.7, 91.3)	41.3 (7.3, 74.0)	0.953
Th1 (cells/ μ L)	99.2 (58.5, 164.1)	164.4 (94.8, 213.2)	84.0 (55.9, 149.8)	0.068
Th1 (% WB)	19.4 (16.3, 25.8)	28.1 (22.0, 33.2)	18.6 (16.2, 23.0)	0.006**
Th2 (cells/ μ L)	38.4 (24.7, 62.2)	26.5 (16.4, 70.1)	42.6 (26.0, 62.2)	0.251
Th2 (% WB)	8.3 (5.7, 11.1)	6.4 (5.1, 10.0)	8.7 (5.9, 11.7)	0.181
Th17 (cells/ μ L)	25.9 (15.9, 40.3)	25.8 (13.6, 34.0)	25.9 (16.0, 41.3)	0.665
Th17 (% WB)	5.1 (4.0, 7.5)	4.3 (3.6, 5.7)	5.3 (4.1, 8.1)	0.112
Treg (cells/ μ L)	23.7 (14.0, 35.0)	25.5 (21.9, 35.3)	22.5 (13.9, 35.0)	0.394
Treg (% WB)	5.3 (3.7, 8.1)	5.2 (3.6, 6.4)	5.3 (3.8, 8.5)	0.830
Th1/Th2 (cells/ μ L)	2.4 (1.6, 4.3)	6.1 (2.4, 8.3)	2.2 (1.5, 3.3)	0.005**
Th1/Th2 (% WB)	2.3 (1.6, 4.0)	4.5 (1.9, 6.4)	2.2 (1.6, 3.4)	0.033*
Th17/Treg (% WB)	1.0 (0.7, 1.3)	0.8 (0.7, 1.0)	1.0 (0.8, 1.4)	0.150
Th1/Th17 (% WB)	3.8 (2.3, 6.0)	6.5 (3.6, 8.8)	3.6 (2.1, 5.5)	0.009**
T cells (% WB)	16.0 (10.1, 21.9)	17.2 (11.7, 25.8)	15.6 (10.0, 20.5)	0.634
CD4 T-cells (cells/ μ L)	486.0 (291.9, 644.3)	574.0 (271.3, 883.4)	475.9 (292.9, 637.9)	0.550
CD8 T-cells (cells/ μ L)	135.9 (77.0, 272.8)	161.7 (58.9, 300.4)	118.8 (77.3, 181.6)	0.419
CD4/CD8 ratio	3.2 (2.2, 4.8)	2.5 (2.0, 5.8)	3.7 (2.2, 4.8)	0.372
Monocytes (% WB)	8.5 (7.0, 10.5)	8.7 (8.2, 10.6)	8.4 (6.7, 10.4)	0.370
IL5 (pg/mL)	1.5 (1.1, 2.1)	1.7 (1.2, 2.1)	1.5 (1.1, 2.2)	0.707
TNF- α (pg/mL)	1.0 (0.3, 2.0)	1.8 (1.0, 2.4)	0.7 (0.3, 1.8)	0.062
IL4 (pg/mL)	4.3 (3.6, 5.1)	4.6 (3.6, 5.1)	3.9 (3.6, 5.1)	0.421
IL6 (pg/mL)	0.8 (0.2, 1.8)	1.2 (0.6, 2.0)	0.6 (0.2, 1.5)	0.155
IL33(pg/mL)	4.9 (2.2, 6.3)	3.9 (2.2, 5.3)	5.4 (2.8, 6.5)	0.290
IL10 (pg/mL)	1.3 (-0.3, 2.2)	1.7 (0.5, 2.2)	0.9 (-0.3, 1.5)	0.534
IFN- γ (pg/mL)	4.7 (2.9, 6.5)	5.1 (2.5, 6.5)	4.6 (3.1, 6.5)	0.887

¹Median (Q1, Q3)

²Kruskal-Wallis rank sum test

³Percentages were calculated among non-missing observations. Missing data were minimal (<5%) across variables.

Extra materials

Table 3
Demographics, clinical characteristics, and immunophenotyping of participants with COPD exacerbations

Variable	Overall (n = 95 ¹)	ECOPD (n = 13 ¹)	Stable (n = 82 ¹)	P-value ²
Age (years)	70.2 ± 6.9	70.8 ± 6.1	70.1 ± 7.1	0.919
Female	40 (42%)	7 (54%)	33 (40%)	0.381
Race				0.623
White	63 (66%)	10 (77%)	53 (65%)	
Black or African American	25 (26%)	2 (15%)	23 (28%)	
Asian	5 (5.3%)	1 (7.7%)	4 (4.9%)	
Other	2 (2.1%)	0 (0%)	2 (2.4%)	
BMI (kg/m2)	26.9 ± 5.0	25.1 ± 4.3	27.2 ± 5.0	0.201
Smoking pack years	47.2 ± 32.2	49.5 ± 39.9	46.9 ± 31.1	0.852
Current smoker	25 (26%)	8 (62%)	17 (21%)	0.004**
Home O2	9 (11%)	2 (18%)	7 (9.9%)	0.347
Asthma history	29 (31%)	4 (36%)	25 (30%)	0.735
Emphysema	16 (20%)	7 (88%)	9 (13%)	<0.001***
Cardiovascular disease	55 (59%)	6 (50%)	49 (60%)	0.546
LABA	4 (5.9%)	0 (0%)	4 (6.8%)	>0.999
LAMA	30 (41%)	4 (36%)	26 (42%)	>0.999
ICS	7 (10%)	1 (11%)	6 (10%)	>0.999
ESR (mm/h)	25.6 ± 22.4	35.5 ± 35.1	24.1 ± 19.7	0.341
Fibrinogen (mg/dL)	363.7 ± 98.4	445.6 ± 155.0	352.4 ± 83.3	0.024*
CRP (mg/dL)	1.5 ± 4.1	6.3 ± 10.0	0.8 ± 1.3	<0.001***
WBC (×10 ⁹ /μL)	7.9 ± 4.5	12.2 ± 5.2	7.3 ± 4.1	<0.001***
Th1 (cells/μL)	91.1 (58.5, 163.2)	66.6 (58.5, 91.2)	99.2 (58.5, 164.1)	0.593
Th1 (% WB)	21.0 (16.5, 27.5)	28.8 (26.9, 31.9)	19.4 (16.3, 25.8)	0.014*
Th2 (cells/μL)	33.1 (22.7, 56.3)	14.5 (9.2, 41.7)	38.4 (24.7, 62.2)	0.027*
Th2 (% WB)	8.1 (5.4, 10.5)	5.2 (4.7, 7.5)	8.3 (5.7, 11.1)	0.057
Th17 (cells/μL)	24.4 (15.5, 39.7)	17.7 (7.6, 39.0)	25.9 (15.9, 40.3)	0.266
Th17 (% WB)	5.1 (4.0, 7.3)	5.2 (3.9, 7.2)	5.1 (4.0, 7.5)	0.779
Treg (cells/μL)	21.9 (13.4, 33.9)	10.1 (3.6, 18.7)	23.7 (14.0, 35.0)	0.015*
Treg (% WB)	5.2 (3.6, 7.5)	2.9 (0.8, 6.1)	5.3 (3.7, 8.1)	0.040*
Th1/Th2 (% WB)	2.5 (1.8, 4.7)	4.9 (3.2, 5.4)	2.3 (1.6, 4.0)	0.02*
Th1/Th17 (%WB)	3.8 (2.5, 6.1)	5.2 (3.7, 7.7)	3.8 (2.3, 6.0)	0.155
Neutrophils (% WB)	66.6 (58.8, 72.7)	81.7 (73.3, 88.7)	65.9 (57.4, 71.1)	<0.001***
Lymphocyte (% WB)	20.1 (16.3, 29.2)	10.5 (6.1, 18.3)	21.9 (16.9, 29.3)	0.001***
Eosinophils (% WB)	2.0 (1.3, 3.1)	0.7 (0.0, 1.9)	2.2 (1.4, 3.3)	0.003**
Blood Eosinophils (cells/μL)	144.6 (82.1, 253.1)	599.9 (0.0, 1,173.2)	138.8 (82.1, 211.1)	0.043*
Neutrophil-to-lymphocyte ratio	4.5 ± 5.0	10.7 ± 10.0	3.6 ± 3.0	<0.001***
IL5 (pg/mL)	1.6 (1.1, 2.3)	6.9 (5.3, 8.4)	1.5 (1.1, 2.1)	0.018*
TNF-α (pg/mL)	2.1 (1.3, 3.9)	3.7 (1.5, 6.6)	2.1 (1.2, 3.9)	0.186
IL4 (pg/mL)	20.2 (12.1, 40.7)	78.3 (20.0, 165.9)	20.2 (12.1, 35.4)	0.096
IL6 (pg/mL)	2.0 (1.2, 3.9)	4.8 (3.1, 7.4)	1.7 (1.2, 3.6)	0.014*
IL33(pg/mL)	29.7 (6.8, 76.5)	52.8 (20.2, 84.5)	29.7 (4.5, 76.5)	0.232
IL10 (pg/mL)	2.6 (0.8, 4.6)	3.3 (0.8, 5.0)	2.4 (0.8, 4.6)	0.839
IFN-γ (pg/mL)	33.9 (10.7, 91.0)	72.8 (52.2, 107.1)	26.8 (7.7, 91.0)	0.13

¹Median (Q1, Q3); n (%); mean ± SD

No difference in cytokine patterns in peripheral blood CB and non-CB groups.

Variable	Overall (n = 82 ¹)	CB (n = 19 ¹)	Non-CB (n = 63 ¹)	P-value ²
CRP (mg/dL)	0.3 (0.3, 0.6)	0.4 (0.3, 1.1)	0.3 (0.3, 0.5)	0.115
IL5 (pg/mL)	1.5 (1.1, 2.1)	1.7 (1.2, 2.1)	1.5 (1.1, 2.2)	0.707
TNF- α (pg/mL)	1.0 (0.3, 2.0)	1.8 (1.0, 2.4)	0.7 (0.3, 1.8)	0.062
IL4 (pg/mL)	4.3 (3.6, 5.1)	4.6 (3.6, 5.1)	3.9 (3.6, 5.1)	0.421
IL6 (pg/mL)	0.8 (0.2, 1.8)	1.2 (0.6, 2.0)	0.6 (0.2, 1.5)	0.155
IL33(pg/mL)	4.9 (2.2, 6.3)	3.9 (2.2, 5.3)	5.4 (2.8, 6.5)	0.290.
IL10 (pg/mL)	1.3 (-0.3, 2.2)	1.7 (0.5, 2.2)	0.9 (-0.3, 1.5)	0.534
IFN- γ (pg/mL)	4.7 (2.9, 6.5)	5.1 (2.5, 6.5)	4.6 (3.1, 6.5)	0.887

- Cytokine shifts or patterns may be compartmentalized
- Potential confounds in cytokine analysis

Table 4
Blood eosinophilia and relationship with Type 1 immunity in CB

Variable	Overall COPD Cohort (n=58) ³			Chronic Bronchitis Cohort (n=15) ³		
	BEC<300 N = 49 ¹	BEC≥300 N = 10 ¹	P-value ²	BEC<300 N = 13 ¹	BEC≥300 N = 2 ¹	P-value ²
Th1 (cells/μL)	86.0 (55.9, 166.5)	108.0 (72.5, 149.8)	0.808	166.5 (91.0, 230.1)	117.4 (72.5, 162.3)	0.497
Th1 (% WB)	19.4 (16.3, 25.6)	19.9 (16.4, 27.7)	0.642	30.5 (23.7, 33.6)	27.0 (23.1, 30.8)	0.610
Th2 (cells/μL)	42.6 (25.9, 56.4)	28.6 (22.1, 62.2)	0.467	27.2 (13.1, 56.2)	15.0 (7.9, 22.1)	0.174
Th2 (% WB)	8.5 (5.9, 11.7)	7.5 (4.2, 10.4)	0.342	8.1 (5.9, 10.8)	3.3 (2.5, 4.2)	0.027*
Th17 (cells/μL)	25.1 (16.0, 34.6)	36.0 (12.9, 51.9)	0.284	27.9 (17.7, 34.6)	17.7 (12.0, 23.4)	0.308
Th17 (% WB)	4.8 (4.0, 6.4)	7.9 (4.5, 9.7)	0.069	5.2 (3.9, 5.7)	4.1 (3.8, 4.5)	0.396
Treg (cells/μL)	22.2 (13.7, 31.5)	30.9 (23.3, 48.7)	0.070	25.5 (16.7, 40.3)	29.3 (23.3, 35.3)	0.865
Treg (% WB)	4.9 (3.6, 7.7)	7.2 (5.7, 9.0)	0.056	5.0 (3.6, 6.4)	7.7 (5.7, 9.7)	0.234
Th1/Th2 (% WB)	2.3 (1.7, 3.8)	2.5 (1.6, 6.8)	0.322	3.1 (1.9, 6.0)	8.3 (7.4, 9.2)	0.027*
Th17/Treg (% WB)	1.0 (0.7, 1.3)	0.9 (0.8, 1.8)	0.773	1.0 (0.8, 1.4)	0.6 (0.4, 0.8)	0.126
Th1/Th17 (% WB)	3.9 (2.5, 5.9)	2.9 (1.9, 6.0)	0.275	5.2 (3.6, 7.4)	6.5 (6.0, 6.9)	0.610

¹Median (Q1, Q3)

²Kruskal-Wallis rank sum test

³Analyses include only participants with non-missing Th1 measurements. Percentages were calculated among non-missing observations. Missing data were minimal (<5%) across variables.

Methods: Statistical Analysis

 Descriptive statistics: mean $\pm$ SD or median (IQR)

↕ Between-group comparisons: Kruskal–Wallis, Fisher's exact

 Correlations: Spearman rank correlation

 Association with CB: multivariable logistic regression

- Adjusted covariates: age, sex, race, smoking, pack-years, ESR, FEV₁

1. Compare CB vs non-CB groups

2. Characterize relationship between variables

3. Determine if CB predicts an inflammatory profile

Table 4
Blood eosinophilia and relationship with Type 1 immunity in CB

Variable	Overall COPD Cohort (n=58) ³			Chronic Bronchitis Cohort (n=15) ³		
	BEC<300	BEC≥300	P-value ²	BEC<300	BEC≥300	P-value ²
	N = 49 ¹	N = 10 ¹		N = 13 ¹	N = 2 ¹	
Th1 (cells/μL)	86.0 (55.9, 166.5)	108.0 (72.5, 149.8)	0.808	166.5 (91.0, 230.1)	117.4 (72.5, 162.3)	0.497
Th1 (% WB)	19.4 (16.3, 25.6)	19.9 (16.4, 27.7)	0.642	30.5 (23.7, 33.6)	27.0 (23.1, 30.8)	0.610
Th2 (cells/μL)	42.6 (25.9, 56.4)	28.6 (22.1, 62.2)	0.467	27.2 (13.1, 56.2)	15.0 (7.9, 22.1)	0.174
Th2 (% WB)	8.5 (5.9, 11.7)	7.5 (4.2, 10.4)	0.342	8.1 (5.9, 10.8)	3.3 (2.5, 4.2)	0.027*
Th17 (cells/μL)	25.1 (16.0, 34.6)	36.0 (12.9, 51.9)	0.284	27.9 (17.7, 34.6)	17.7 (12.0, 23.4)	0.308
Th17 (% WB)	4.8 (4.0, 6.4)	7.9 (4.5, 9.7)	0.069	5.2 (3.9, 5.7)	4.1 (3.8, 4.5)	0.396
Treg (cells/μL)	22.2 (13.7, 31.5)	30.9 (23.3, 48.7)	0.070	25.5 (16.7, 40.3)	29.3 (23.3, 35.3)	0.865
Treg (% WB)	4.9 (3.6, 7.7)	7.2 (5.7, 9.0)	0.056	5.0 (3.6, 6.4)	7.7 (5.7, 9.7)	0.234
Th1/Th2 (% WB)	2.3 (1.7, 3.8)	2.5 (1.6, 6.8)	0.322	3.1 (1.9, 6.0)	8.3 (7.4, 9.2)	0.027*
Th17/Treg (% WB)	1.0 (0.7, 1.3)	0.9 (0.8, 1.8)	0.773	1.0 (0.8, 1.4)	0.6 (0.4, 0.8)	0.126
Th1/Th17 (% WB)	3.9 (2.5, 5.9)	2.9 (1.9, 6.0)	0.275	5.2 (3.6, 7.4)	6.5 (6.0, 6.9)	0.610

¹Median (Q1, Q3)
²Kruskal-Wallis rank sum test
³Analyses include only participants with non-missing Th1 measurements. Percentages were calculated among non-missing observations. Missing data were minimal (<5%) across variables.