Supplementary Table 1. Pathogen-associated molecular patterns (PAMPs) and corresponding Toll-like receptors that recognize each PAMP and the assigned study ID used in the protocol for each PAMP concentration.

PAMP	Toll-like Receptor	Concentration	Assigned study PAMP ID #
Media	NA	NA	4
		Pam3Cys at 10 ng/ml	5
Pam3Cys	TLR1/TLR2	Pam3Cys at 100 ng/ml	6
		Zymosan at 10 mcg/ml	19
Zymosan	TLR2/TLR6	Zymosan at 100 mcg/ml	20
		FSL at 10 ng/ml	21
Dyacylated lipoprotein (Pam2)	TLR2/TLR6	FSL at 100 ng/ml	22
		O111:B4 at 0.1 ng/ml	32
Smooth form LPS from E. Coli	TLR4	O111:B4 at 1 ng/ml	23
	I LIV	O111:B4 at 10 ng/ml	1
Rough form LPS from salmonella		Re595UP at 0.01 ng/ml	33
Rough form Er o nom samonena	TLR4	Re595UP at 0.1 ng/ml	27
		Re595UP at 1 ng/ml	11
Flagellin from S. typhimurium	TLR5	Flagellin at 100 ng/ml	2
Imidazoquinoline compound from	TI D7/TI D0	R848 at 0.1 µM	25
RNA	TLR7/TLR8	R848 at 1 µM	26

Supplementary Figure 1: Heat map showing models with a false discovery rate < 0.10 comparing cytokine levels for subjects with and without severe COPD or chronic bronchitis for each PAMP-cytokine level pair*.

			Severe COPD associated with <u>higher</u> cytokine														
	PAMP	TNF-α	IL-6	IL-8	IL-10	II-1RA	GCSF	IL1B	MCP1	TNF-a	IL-6	IL-8	IL-10	II-1RA	GCSF	IL1B	MCP
	Media																
COPD severity	Pam3Cys at 10 ng/ml																
	Pam3Cys at 100 ng/ml																
	Zymosan at 10 mcg/ml																
	Zymosan at 100 mcg/ml																
	FSL at 10 ng/ml																
	FSL at 100ng/ml																
COPD seventy	O111:B4 at 0.1 ng/ml																
	O111:B4 at 1 ng/ml																
	O111:B4 at 10 ng/ml																
	Re595UP at 0.01mg/ml																
	Re595UP at 0.1mg/ml																
	Re595UP at 1mg/ml																
	Flagellin																
	R848 at 0.1 microM																
	R848 at 1 microM																
	Chronic bronchitis associated with <u>lower</u> cytokine levels Chronic bronchitis associated with <u>higher</u> cytokine levels																
		Cilionic	pronci	nitis ass	ociated	with <u>lo</u>	<i>ver</i> cyto	okine le	evels	Chronic	: bronch	nitis asso	ociated	with <u>hic</u>	<u>iher</u> cyt	okine le	veis
	PAMP	TNF-a	IL-6	IL-8		with <u>lo</u>		IL1B	MCP1	Chronic TNF-a	lL-6	itis asso	IL-10	with <u>hig</u> II-1RA	<u>iher</u> cyto GCSF	IL1B	,
	Media																,
	Media Pam3Cys at 10 ng/ml																,
	Media Pam3Cys at 10 ng/ml Pam3Cys at 100 ng/ml																
	Media Pam3Cys at 10 ng/ml Pam3Cys at 100 ng/ml Zymosan at 10 mcg/ml																
	Media Pam3Cys at 10 ng/ml Pam3Cys at 100 ng/ml Zymosan at 10 mcg/ml Zymosan at 100 mcg/ml																
	Media Pam3Cys at 10 ng/ml Pam3Cys at 100 ng/ml Zymosan at 10 mcg/ml Zymosan at 100 mcg/ml FSL at 10 ng/ml																,
Chronic bronchitis	Media Pam3Cys at 10 ng/ml Pam3Cys at 100 ng/ml Zymosan at 10 mcg/ml Zymosan at 100 mcg/ml FSL at 10 ng/ml FSL at 100ng/ml																,
Chronic bronchitis	Media Pam3Cys at 10 ng/ml Pam3Cys at 100 ng/ml Zymosan at 10 mcg/ml Zymosan at 100 mcg/ml FSL at 10 ng/ml FSL at 100ng/ml O111:B4 at 0.1 ng/ml																,
Chronic bronchitis	Media Pam3Cys at 10 ng/ml Pam3Cys at 100 ng/ml Zymosan at 10 mcg/ml Zymosan at 100 mcg/ml FSL at 10 ng/ml FSL at 100ng/ml O111:B4 at 0.1 ng/ml O111:B4 at 1 ng/ml																,
Chronic bronchitis	Media Pam3Cys at 10 ng/ml Pam3Cys at 100 ng/ml Zymosan at 10 mcg/ml Zymosan at 100 mcg/ml FSL at 10 ng/ml FSL at 100ng/ml O111:B4 at 0.1 ng/ml O111:B4 at 1 ng/ml O111:B4 at 10 ng/ml																
Chronic bronchitis	Media Pam3Cys at 10 ng/ml Pam3Cys at 100 ng/ml Zymosan at 10 mcg/ml Zymosan at 100 mcg/ml FSL at 10 ng/ml FSL at 100ng/ml O111:B4 at 0.1 ng/ml O111:B4 at 1 ng/ml O111:B4 at 10 ng/ml Re595UP at 0.01mg/ml																
Chronic bronchitis	Media Pam3Cys at 10 ng/ml Pam3Cys at 100 ng/ml Zymosan at 10 mcg/ml Zymosan at 100 mcg/ml FSL at 10 ng/ml FSL at 100ng/ml O111:B4 at 0.1 ng/ml O111:B4 at 1 ng/ml O111:B4 at 10 ng/ml Re595UP at 0.01mg/ml																
Chronic bronchitis	Media Pam3Cys at 10 ng/ml Pam3Cys at 100 ng/ml Zymosan at 10 mcg/ml Zymosan at 100 mcg/ml FSL at 10 ng/ml FSL at 100ng/ml O111:B4 at 0.1 ng/ml O111:B4 at 1 ng/ml O111:B4 at 10 ng/ml Re595UP at 0.01mg/ml Re595UP at 0.1mg/ml																,
Chronic bronchitis	Media Pam3Cys at 10 ng/ml Pam3Cys at 100 ng/ml Zymosan at 10 mcg/ml Zymosan at 100 mcg/ml FSL at 10 ng/ml FSL at 100ng/ml O111:B4 at 0.1 ng/ml O111:B4 at 1 ng/ml O111:B4 at 10 ng/ml Re595UP at 0.01mg/ml																MCP2

^{*} Each square corresponds to the q-value for one t-test comparing cytokine levels after stimulation with a PAMP between subjects with and without chronic bronchitis. For example the square in the upper right corner shows the q-value for the t-test comparing MCP-1 levels in response to media (no PAMP) between those with and without chronic bronchitis

Q-value < 0.10 ≥0.10

Supplementary Figure 2: Heat map showing the strength of tests of associations comparing cytokine levels for subjects using inhaled steroids and those not using inhaled steroids for each PAMP-cytokine level pair stratified by inhaled steroid use.*

P-value range
< 0.01
0.01-0.05
0.05-0.1
0.1-0.15
0.15-0.20
>0.2

Inhaled steroids associated with <u>lower</u> cytokine levels**								Inhaled steroids associated with <u>higher</u> cytokine levels								
PAMP	TNF-a	IL-6	IL-8	IL-10	II-1RA	GCSF	IL1B	MCP1	TNF-a	IL-6	IL-8	IL-10	II-1RA	GCSF	IL1B	MCP1
Media																
Pam3Cys at 10 ng/ml																
Pam3Cys at 100 ng/ml																
Zymosan at 10 mcg/ml																
Zymosan at 100 mcg/ml																
FSL at 10 ng/ml																
FSL at 100ng/ml																
O111:B4 at 0.1 ng/ml																
O111:B4 at 1 ng/ml																
O111:B4 at 10 ng/ml																
Re595UP at 0.01mg/ml																
Re595UP at 0.1mg/ml																
Re595UP at 1mg/ml																
Flagellin							Ţ									
R848 at 0.1 microM																
R848 at 1 microM																

^{*} Each square corresponds to the p-value for one t-test comparing cytokine levels after stimulation with a PAMP between subjects with and without severe COPD. For example the square in the upper right corner shows the P-value for the t-test comparing MCP-1 levels in response to media (no PAMP) between those with and without severe COPD.

^{**} t-test comparing the mean log-transformed cytokine values for a given PAMP between subjects with and without severe COPD

Supplementary Figure 3: Heat map showing the strength of tests of associations comparing cytokine levels for subjects with and without severe COPD for each PAMP-cytokine level pair stratified by inhaled steroid use.*

