

N=6 3 to 55mo	Right middle lobe vs. lingula		NS			NS	Paired t-test	[4], svBAL, F
N=12 24±2yr	Upper lobe vs. lower lobe	p<0.01 Upper: 2.6±0.8x10 ⁶ /mL vs. Lower: 0.7±0.3x10 ⁶ /mL	p<0.01 Upper: 71.1±5.6 vs. Lower: 46.6±7.3	p<0.01 Upper: 227±91 nmol/min/mL vs. Lower: 84±43nmol/min/mL			Paired t-test, Mean±SD	[5], P
N=8 FEV ₁ ≥65%, 24±3yr	Upper lobe vs. lower lobe	p<0.05 Upper: 1.4±0.4x10 ⁶ /mL vs. Lower: 0.2±0.08x10 ⁶ /mL	p<0.05 Upper: 67.9±8.1 vs. Lower: 37.5±9.0	p<0.05 Upper: 106±37nmol/min/mL vs. Lower: 15±8nmol/min/mL			Paired t-test, Mean±SD	[5], P
N=4 FEV ₁ ≤50%, 23±2yr	Upper lobe vs. lower lobe	NS	NS	NS			Paired t-test	[5], P

Table E2: Convergent validity					
Cross sectional correlation between BAL inflammatory markers					
N (n)	Age	Comparison	Results	Statistics	Author
16	0.08 to 0.97yr	PMN count vs. IL-8	r=0.76, p=0.0018	Not reported	[6], P

16	86 (18 to 167) wk	PMN% vs. IL-8	$r=0.86, p<0.001$	Not reported	[7], ns
46 CF	<24mo	PMN count vs. IL-8	$r=0.61, p<0.001$	Spearman	[8], svBAL, F
13 non-CF	11.7±10.2mo	PMN count vs. NE	$r=0.55, p<0.001$		
		IL-8 vs. NE	$r=0.56, p<0.001$		
24 (27)	<6yrs	Total cell burden vs. IL-8	$r^2=0.676, p<0.001$	Generalised estimating equation	[9], F (microbiology), P (aliquots 2 & 3)
		PMN count vs. IL-8	$r^2=0.729, p<0.001$		
14	<7yr	PMN count vs. IL-8	$r=0.79, p=0.0001$	Spearmans	[10], ns
18	12 to 36yr	PMN count vs. NE	NS	Pearson	[11], P
22	20±2yr	PMN count vs. IL-8	NS	Regression analysis	[12], P
22	20±2yr	NE vs. IL-8	NS	Regression analysis	[12], P
22	20±2yr	IL-8 vs. total cells	NS	Regression analysis	[12], P
12	24±2yr	PMN count vs. NE	$r=0.82$	Regression analysis	[5], P

14	17 to 40yr	PMN count vs. NE (during exacerbation)	p<0.05	Not reported	[13], P
34	24 to 58 yr CF and non-CF patients	PMN % (BAL) vs. IL-8 (BAL)	r = 0.764, p < 0.001	Linear Regression	[14], P
Cross sectional correlation between BAL inflammatory markers and sputum, nasal wash, biopsy or serum inflammatory markers					
19	1.9 (< 6 yrs)	IL-8 (BAL) vs. IL-8 (Nasal Wash)	r ² = 0.48; p = 0.036	Pearson	[15], P
19	1.9 (< 6 yrs)	PMN % (BAL) vs. PMN (Nasal Wash)	r ² = 0.70; p = 0.004	Pearson	[15], P
46	7.8 (0.2 to 16.8)yr	PMN (BAL) vs. PMN (airway biopsy)	NS	Pearson	[16], P
5	8(4 to 18)yr	IL-8 (BAL) vs. IL-8 (spontaneous sputum)	r=0.967, p=0.007	Not reported	[17],svBAL, F
		IL-8 (BAL) vs. IL-8 (serum)	NS		
11	17 to 40yr	PMN count vs. NE/α1-antiprotease	r=0.59, p=0.01	Not reported	[14], P

		complex (serum)			
34	24 to 58 yr <i>CF and non-CF patients</i>	Cell type (BAL) vs. cell type (induced sputum)	NS	Linear Regression	[14], P
		IL-8 (BAL) vs. IL-8 (induced sputum)	Higher BAL % neutrophilia (x4) and IL-8 (x3) in obliterative bronchiolitis syndrome (BOS); NS in sputum	Student's <i>t</i> -test	
31	>18 yrs <i>CF and non-CF patients</i>	IL-8 (BAL) vs. IL-8 (induced sputum)	NS	Spearman	[18], F
			Higher in induced sputum than BAL: Median: 19,860 vs. 3,855 pg/ml	ANOVA	

Table E3: Correlation between BAL inflammatory markers and other outcome measures in people with CF							
N (n)	Age	Comparison	Results				Author
			PMN counts	PMN %	NE	IL-6	
Cross sectional correlation with FEV ₁							

28	19.8 (15.5 to 23.4)wk	FEV _{0.5}	NS		p=0.001. Each doubling in the levels of NE was associated with a 0.46 reduction in FEV _{0.5} z-scor		NS	[19], F, P (2 & 3)
43	6.2 (0.3 to 16.8)yr	FEV ₁			r=-0.44, p<0.05			[20], P
29	7.8 (0.2 to 16.8)	FEV ₁	NS					[16], P
18	20±1yr	FEV ₁	NS					[11], P
22	20±2yr	FEV ₁					NS	[12], P
12	24±2yr	FEV ₁	r=-0.68			r=-0.58		[5], P
Cross sectional correlation with other measures of respiratory function								
28	19.8 (15.5 to 23.4)wk	FVC	NS		p=0.003. Each doubling in the levels of NE was associated with a 0.55 reduction in FVC z-score		NS	[19], F, P (2 & 3)
40 (109)	≤15mo at study entry	VmaxFRC	NS				NS	[21], ns
40 (109)	≤15mo at study entry	FRC	NS				NS	[21], ns
22	23.2mo	FRC/TLC	r=0.50, p=0.02				r=0.45, p=0.04	[22], F
22	23.2mo	respiratory system compliance		r=-0.51, p=0.017				[22], F

16	86 (18 to 167)wk	FEF ₇₅		$r=-0.67, p<0.01$			NS	[7], ns
16	86 (18 to 167)wk	FEF ₂₅₋₇₅		$r=-0.67, p<0.01$			NS	[7], ns
16	86 (18 to 167)wk	FRC		$r=0.66, p<0.01$				[7], ns
16	86 (18 to 167)wk	FRC/TLC		$r=0.574, p<0.05$				[7], ns
16	86 (18 to 167)wk	RV/TLC		$r=0.574, p<0.05$				[7], ns
24 (27) CF	1.58 (IQR:1.07 to 2.75)y	tissue damping (LFFOT)	$Z=2.62, p<0.009$				$Z=2.43, p=0.024$	[9], F (microbiology), P (aliquots 2 & 3)
24 (27) CF	1.58 (IQR:1.07 to 2.75)y	tissue resistance (LFFOT)		$Z=2.09, p<0.036$				[9], F (microbiology), P (aliquots 2 & 3)

24 (27) CF	1.58 (IQR:1.07 to 2.75)y	ratio of damping to elastance (LFFOT)	Z=3.63, p<0.001	Z=3.03, p=0.002			Z=3.31, p=0.001	[9], F (microbiology), P (aliquots 2 & 3)
29	7.8 (0.2 to 16.8)	FVC	NS					[16], P
29	7.8 (0.2 to 16.8)	FEV ₁ /FVC	NS					[16], P
14	17 to 40yr	FEV ₁ (during exacerbation)			r=0.62, p=0.02			[13], P
14	17 to 40yr	FEV ₁ /FVC (during exacerbation)			r=0.80, p<0.001			[13], P

Cross sectional correlation with measures of imaging

57	3.6 (IQR:2.3 to 4.9)mo	bronchial dilatation presence	OR(95%CI) = 17.3(2.0 to 148.7), p=0.009	NS	OR(95%CI) = 10.9(2.5 to 46.7), p=0.001		OR(95%CI) = 3.7(1.0 to 13.5), p=0.047	[23], F, P (2 & 3)
57	3.6 (IQR:2.3 to 4.9)mo	bronchial dilatation extent	OR(95%CI) = 33.8(3.1 to 363.2), p=0.004	NS	OR(95%CI) = 10.8(3.0 to 38.8), p=0.001		NS	[23], F, P (2 & 3)
57	3.6 (IQR:2.3 to 4.9)mo	bronchial wall thickening presence	NS	NS	OR(95%CI) = 9.4(1.7 to 52.3), p=0.01		NS	[23], F, P (2 & 3)
57	3.6 (IQR:2.3 to 4.9)mo	bronchial wall thickening extent	NS	NS	OR(95%CI) = 4.3(1.7 to 10.7), p=0.002		NS	[23], F, P (2 & 3)
57	3.6 (IQR:2.3 to 4.9)mo	air trapping presence	NS	NS	NS		NS	[23], F, P (2 & 3)
57	3.6 (IQR:2.3 to 4.9)mo	air trapping extent	NS	NS	OR(95%CI) = 3.9(1.6 to 9.9), p=0.004		NS	[23], F, P (2 & 3)

16	0.48 (0.08 to 0.97)yr	Wisconsin chest x-ray score	NS					[6], P
40 (109)	≤15mo at study entry	Brasfield score	NS				NS	[21], ns
Cross sectional correlation with measures of anthropometrics								
36	At diagnosis, 1yr, 2yr, 3yr	ΔBMI	NS		p=0.022. Each log10 increase in NE was associated with a 0.43 (95% CI 0.06 to 0.79) reduction in BMI z-score,	NS	NS	[24], F, P (2 & 3)
16	0.48 (0.08 to 0.97)yr	Weight-for-age	NS					[6], P
40 (109)	≤15mo at study entry	weight percentile	NS				NS	[21], ns
40 (109)	≤15mo at study entry	height percentile	NS				NS	[21], ns
12	24±2yr	% ideal body weight	r=-0.60					[5], P
Cross sectional correlation with measures of microbiology								
16	0.48 (0.08 to 0.97)yr	any culture	p<0.001		p=0.002		p<0.001	[6], P
22	23.2mo	bacterial load		r=0.88, p<0.0001			r=0.61, p<0.03	[22], F
111	6mo to 6yr	P. Aeruginosa + S. Aureus density	r=0.60, p<0.001				r=0.59, p<0.001	[25], P
24 (27) CF	<6yr	bacterial load	p<0.001 (r = not specified)	p<0.001 (r = not specified)				[9], F (microbiology), P (aliquots 2 & 3)

28	1.8yr (3wk to 13yr)	bacterial load	p<0.05 (r = not specified). In this more heavily infected group, the neutrophil to bacteria ratio was 4.9+/-2.3 for CF vs. 2.3+/-2.0 for control samples (p = 0.02)				p=0.016 (r = not specified). IL-8 to bacteria ratio was 0.08+/-0.07 in CF v. 0.003+/-0.0008 in control samples (p =0.01)	[26], ns
18	20±1yr	P. Aeruginosa presence or density	NS					[11], P
14	17 to 40yr	P. Aeruginosa density	NS		NS			[13], P
Cross sectional correlation with other clinical measures								
16	0.48 (0.08 to 0.97)yr	SaO ₂	r=-0.54, p=0.0378					[6], P
16	0.48 (0.08 to 0.97)yr	Respiratory rate	NS					[6], P
40 (109)	≤15mo at study entry	Shwachman score	NS				NS	[21], ns
14	29.5 (3.8 to 85)mo	SaO ₂					r=-0.55, p=0.005	[10], ns
46	7.8 (0.2 to 16.8) yr	CFTR genotype	NS					[16], P
5	8 (4 to 18)yr	Shwachman score					r=-0.92	[17], svBAL, F
Cross sectional correlation with other measures								
16	10.5 (2 to 25)mo	DNA levels	r=0.69, p<0.002					[27], P
46	7.8 (0.2 to 16.8) yr	age	r=0.64, p<0.0001					[16], P

43	6.2 (0.3 to 16.8)yr	glycosaminoglycans concentration	r=0.85, p<0.001		r=0.77, p<0.001			[28], P
43	6.2 (0.3 to 16.8)yr	elastin concentration	r=0.82, p<0.001		r=0.72, p<0.001			[28], P
43	6.2 (0.3 to 16.8)yr	collagen concentration	r=0.75, p<0.001		r=0.75, p<0.001			[28], P
29	9.1±1.2yr	TGF-β ₁ (during exacerbation)	r=0.59, p<0.001	r=0.67, p<0.001				[28], P
48	11.1 (5 to 25)yr	DNA		p<0.01				[29], F, P (2 & 3)
22	20±2yr	LTB ₄					NS	[12], P
22	20±2yr	α ₁ -antiprotease inhibitor					NS	[12], P
22	20±2yr	Elastase-α ₁ -PI complex					NS	[12], P
12	24±2yr	myeloperoxidase	r=0.80			r=0.99		[5], P
12	24±2yr	lipopolysaccharide	r=0.67, p<0.0001					[5], P

ΔBMI = change in body mass index; FEF₇₅= forced expiratory flow at 75% of expired volume; FEF₂₅₋₇₅ = mean forced expiratory flow between 25 and 75%; FEV_{0.5} = forced expiratory volume in 0.5 seconds; FEV₁ = forced expiratory volume in one second; FVC = forced vital capacity; FRC =functional residual capacity ; FRC/TLC = ratio of FRC to total lung capacity; LFFOT = low frequency forced oscillation technique; NS=not significant; RV/TLC = ratio of residual volume to total lung capacity; SaO₂ = arterial blood oxygen saturation; VmaxFRC = maximal flow at FRC

Table E4. Reference values for BAL inflammatory markers (cited in validation studies including CF patients)

N (n)	Additional info	Units	Regression equation	Mean	SD	range	95%CI	Limits of normality	Author
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		available		*median	*SE	*IQR				
				**least squares mean						
Neutrophil count										
<i>Non-CF "Normal" Controls</i>										
9	Infants (congenital stridor)	x10 ³ /L	-		4	-	-	1 to 17	-	[30], ns
10	Infants (congenital stridor)	x10 ³ /mL	-		3	-	-	1 to 7	-	[31], svBAL, F
13	Infants (congenital stridor)	x10 ³ /mL	-		7	-	-	2 to 22	-	[8], svBAL, F
13	Infants (congenital stridor)	x10 ³ /mL	-		7	-	-	2 to 22	-	[32], F
7	Controls (no lower airway symptoms), Mean age 5.8yr	x10 ⁶ /mL	-	*0.0	-	-	0.00 to 0.01	-	-	[28], P
7	Adults (normal non-smoking)	x10 ³ /μL	-	0.4	*0.3	-	-	-	-	[33]
20	Adults (never-smoking, age-matched volunteers), right middle lobe	x10 ⁶ /mL	-	0.002	*0.0007	-	-	-	-	[5], P
13	Adults	x10 ⁶ /mL	-	0.09	*0.02	-	-	-	-	[12], P
23	Disease control, uninfected (median age 1.0 yr)	x10 ³ /mL	-		50	*32	-	-	-	[26], ns
<i>Non-CF Disease Controls</i>										

27	Disease control, infected (median age 1.0 yr)	$\times 10^3/\text{mL}$	-		427 *16	-	-	-	[26], ns
12	Infected Control Infants (upper airway obstruction, recurrent or chronic pneumonia, and recurrent or chronic wheezing)	$\times 10^3/\text{mL}$	-	*229	-	1 to 2,976	-	-	[34], P
12	Uninfected Control Infants (upper airway obstruction, recurrent or chronic pneumonia, and recurrent or chronic wheezing)	$\times 10^3/\text{mL}$	-	*10	-	1 to 117	-	-	[34], P
7	PCD, Mean age 9.2yr	$\times 10^6/\text{mL}$	-	*0.3	-	0.05 to 13.76	-	-	[28], P
26	CRD, Mean age 4.8yr	$\times 10^6/\text{mL}$	-	*0.0	-	0.00 to 17.9	-	-	[28], P
CF									
31	Infants and young children with CF and no pathogens	$\text{Log}_{10}/\text{mL}$	-	4.8	0.6	-	-	-	[25], P
45	Infants with CF and no pathogens	$\times 10^3/\text{mL}$	-	*31.3	-	*11.3 to 76.3	-	-	[23], F, P (2 & 3)
30	Children <6yr with CF and no pathogen	$\times 10^3/\text{mL}$	-		114	-	63 to 206	-	[21], ns

29	Children <6yr with CF and 10^5 CFU/mL pathogens	$\times 10^3/\text{mL}$	-		207	-	-	110 to 391	-	[21], ns
12	Clinically stable adults with CF, 50×10^5 cfu/ml of aerobic bacteria, right upper lobe	$\times 10^6/\text{mL}$	-	2.6	*0.8	-	-	-	-	[5], P
12	Clinically stable adults with CF, 50×10^5 cfu/ml of aerobic bacteria, right lower lobe	$\times 10^6/\text{mL}$	-	0.7	*0.3	-	-	-	-	[5], P
8	Clinically stable adults with CF, $\text{FEV}_1 \geq 65\%$, 50×10^5 cfu/ml of aerobic bacteria, right upper lobe	$\times 10^6/\text{mL}$	-	1.4	*0.4	-	-	-	-	[5], P
8	Clinically stable adults with CF, 50×10^5 cfu/ml of aerobic bacteria, $\text{FEV}_1 \geq 65\%$, right lower lobe	$\times 10^6/\text{mL}$	-	0.2	*0.08	-	-	-	-	[5], P
4	Clinically stable adults with CF, 50×10^5 cfu/ml of aerobic bacteria, $\text{FEV}_1 \leq 50\%$, right upper lobe	$\times 10^6/\text{mL}$	-	5.0	*1.8	-	-	-	-	[5], P

4	Clinically stable adults with CF, FEV ₁ ≤50%, 50x10 ⁵ cfu/ml of aerobic bacteria, right lower lobe	x10 ⁶ /mL	-	1.6	*0.6	-	-	-	[5], P
22	Clinically stable adolescents and adults, FEV1 range 23-99%	x10 ⁶ /mL	-	41	10	-	-	-	[12], P
15	1.58 (1.12 to 2.9)yr Uninfected, with CF	X10 ³ /mL	-	*60.03	-	*38.92 to 91.34	-	-	[9], F (microbiology), P (aliquots 2 & 3)
11	Disease control infants and young children (non-CF pulmonary conditions)	X10 ³ /mL	-	6.9	*1.7	-	-	-	[6], P
23	Clinically stable adults	x10 ⁶ /mL	-	0.1	*0.04	0 to 0.6			[11], P
Percentage neutrophils									
<i>Non-CF "Normal" Controls</i>									
19	Infants (congenital stridor)	%	-	8.2	-	-	4.6 to 15	-	[1], F

7	Infants (congenital stridor) Age range 3 to 14 mo	%	-	*7	-	*4 to 14	-	-	[35], F
7	Infants (congenital stridor) Age range 2 to 54 mo	%	-	*7	-	*4 to 30	-	-	[36], F
48	Children without respiratory disease First sample 3 to 15yr	%	-		4	5	0 to 19		[37], F, P (2 & 3)
48	Children without respiratory disease Pooled sample 3 to 15yr	%	-		2	3	0 to 17		[37], F, P (2 & 3)
10	Normal Adults	%	-		1	1	-	-	[38]
20	Adults (never-smoking, age-matched volunteers), right middle lobe	%	-	1.6	* 0.4	-	-	-	[5], P

13	Adults	%			1	*0.3				[12], P
23	Healthy adults	%	-		3	*0.5	0 to 9			[11], P
8	Healthy adult	%	-	0.2		*0.1	-	-	-	[14], P
8	Healthy adult	%	-	0.3		0.4	-	-	-	[13], P
<i>Non-CF Disease Controls</i>										
23	Disease control (other chronic respiratory conditions), uninfected (median age 1.0 yr)	%	-		12	*3	-	-	-	[26], ns
27	Disease control (other chronic respiratory conditions), infected (median age 1.0 yr)	%	-		34	*6	-	-	-	[26], ns
25	Disease control (other chronic respiratory conditions), mean age 15 ± 3mo	%	-	24.8		*5.2	-	-	-	[39], ns
12	Uninfected control Infants (upper airway obstruction,	%	-	*5		-	1 to 51	-	-	[34], P

	recurrent or chronic pneumonia, and recurrent or chronic wheezing)								
12	Infected control Infants (upper airway obstruction, recurrent or chronic pneumonia, and recurrent or chronic wheezing)	%	-	*46	-	1 to 93	-	-	[34], P
38	6.1±0.6yr Non-CF respiratory conditions	%	-	21.8	3.6				[40], P
<i>CF</i>									
39	Infants and young children with CF without infection	%	-		28	-	-	21 to 35	[41], F
31	Infants and young children with CF and no pathogens	%	-	22.1	14.4	-	-	-	[25], P
45	Infants with CF and no pathogens	%	-	*13.5	-	*8.3 to 26.1	-	-	[23], F, P (2 & 3)
15	1.58 (1.12 to 2.9)yr Uninfected, with CF	%	-	*7.3	-	*8.75 to 29.10	-	-	[9], F (microbiology), P (aliquots 2 & 3)
14	Infants and young children with CF and <10 ⁵ CFU/mL pathogens	%	-	24.14	-	-	-	-	[22], F

24	Infants and young children with CF and $<10^5$ CFU/mL pathogens (lingula)	%	-		29	-	-	22 to 36	-	[4], svBAL, F
24	Infants and young children with CF and $<10^5$ CFU/mL pathogens (right middle lobe)	%	-		28	-	-	21 to 35	-	[4], svBAL, F
22	Clinically stable adolescents and adults, FEV1 range 23-99%	%	-		60	5	-	-	-	[12], P
12	Clinically stable adults with CF, FEV ₁ ≤ 50%, 50×10^5 cfu/ml of aerobic bacteria, right upper lobe	%	-	71.1	*5.6	-	-	-	-	[5], P
12	Clinically stable adults with CF, FEV ₁ ≤ 50%, 50×10^5 cfu/ml of aerobic bacteria, right lower lobe	%	-	46.6	*7.3	-	-	-	-	[5], P
8	Clinically stable adults with CF, FEV ₁ ≤ 50%, 50×10^5 cfu/ml of aerobic bacteria, FEV ₁ ≥ 65%, right upper lobe	%	-	67.9	*8.1	-	-	-	-	[5], P

8	Clinically stable adults with CF, FEV ₁ ≤50%, 50x10 ⁵ cfu/ml of aerobic bacteria, FEV ₁ ≥65%, right lower lobe	%	-	37.5	*9.0	-	-	-	[5], P
4	Clinically stable adults with CF, FEV ₁ ≤50%, 50x10 ⁵ cfu/ml of aerobic bacteria, FEV ₁ ≤50%, right upper lobe	%	-	77.6	*3.5	-	-	-	[5], P
4	Clinically stable adults with CF, FEV ₁ ≤50%, 50x10 ⁵ cfu/ml of aerobic bacteria, FEV ₁ ≤50%, right lower lobe	%	-	64.9	*5.9	-	-	-	[5], P
Neutrophil elastase									
<i>Non-CF "Normal" Controls</i>									
19	Infants (congenital stridor)	% with NE activity	-	32	-	-	13 to 57	-	[1], F
13	Infants (congenital stridor)	% with NE activity	-	23	-	-	5 to 54	-	[8], svBAL, F
7	Controls (no lower airway symptoms), Mean age 5.8yr	µm/mL	-	*100	-	100 to 100	-	-	[28], P
7	Adults (normal non-smoking)	µM	-	Not detectable	-	-	-	-	[33]

20	Adults (never-smoking, age-matched volunteers), right middle lobe	nmol/min/mL	-	Not detectable	-	-	-	-	[5], P
13	Adults	μM	-	Not detectable	-	-	-	-	[12], P
<i>Non-CF Disease Controls</i>									
7	PCD, Mean age 9.2yr	μm/mL	-	*180	-	100 to 3,502	-	-	[28], P
26	CRD, Mean age 4.8yr	μm/mL	-	*100	-	100 to 1,297	-	-	[28]; P
<i>CF</i>									
45	Infants with CF and no pathogens	Number (%) patients with NE detectable	-	10 (22.7)	-	-	-	-	[23], F, P (2 & 3)
45	Infants with CF and no pathogens	ng/mL	-	*100	-	-	-	-	[23], F, P (2 & 3)
39	Infants and young children with CF without infection	pg/mL	-	253	-	-	158 to 406	-	[41], F
31	Infants and young children with CF and no pathogens	Number (%) patients with NE detectable	-	0 (0)	-	-	-	-	[25], P
22	Clinically stable adolescents and adults, FEV1 range 23-99%	μM	-	1.9	0.5	-	-	-	[12], P
12	Clinically stable adults with CF, FEV ₁ ≤ 50%, 50x10 ⁵ cfu/ml of aerobic bacteria, right upper lobe	nmol/min/mL	-	227	*91	-	-	-	[5], P

12	Clinically stable adults with CF, FEV ₁ ≤50%, 50x10 ⁵ cfu/ml of aerobic bacteria, right lower lobe	nmol/min/mL	-	84	*43	-	-	-	[5], P
8	Clinically stable adults with CF, FEV ₁ ≤50%, 50x10 ⁵ cfu/ml of aerobic bacteria, FEV ₁ ≥65%, right upper lobe	nmol/min/mL	-	106	*37	-	-	-	[5], P
8	Clinically stable adults with CF, FEV ₁ ≤50%, 50x10 ⁵ cfu/ml of aerobic bacteria, FEV ₁ ≥65%, right lower lobe	nmol/min/mL	-	15	*8	-	-	-	[5], P
4	Clinically stable adults with CF, FEV ₁ ≤50%, 50x10 ⁵ cfu/ml of aerobic bacteria, FEV ₁ ≤50%, right upper lobe	nmol/min/mL	-	470	*235	-	-	-	[5], P
4	Clinically stable adults with CF, FEV ₁ ≤50%, 50x10 ⁵ cfu/ml of aerobic bacteria, FEV ₁ ≤50%, right lower lobe	nmol/min/mL	-	224	*101	-	-	-	[5], P

IL-8

Non-CF "Normal" Controls

9	Infants (congenital stridor)	ng/L	-	23	-	-	8 to 62	-	[30], ns
10	Infants (congenital stridor)	pg/mL	-	27	-	-	10 to 45	-	[31], svBAL, F
13	Infants (congenital stridor)	pg/mL	-	32	-	-	12 to 84	-	[8], svBAL, F
13	Infants (congenital stridor)	pg/mL	-	32	-	-	12 to 84	-	[32], F
19	Infants (congenital stridor)	pg/mL	-	24	-	-	12 to 47	-	[1], F
7	Infants (congenital stridor) Age range 3 to 14 mo	pg/mL	-	*15	-	*4 to 24	-	-	[35], F
7	Infants (congenital stridor) Age range 3 to 14 mo	pg/mL	-	*10	-	*4 to 23	-	-	[36], F
7	Controls (no lower airway symptoms), Mean age 5.8yr	pg/mL	-	*64	-	31 to 221	-	-	[28], P
7	Adults (normal non-smoking)	nM	-	Not detectable	-	-	-	-	[33]
<i>Non-CF Disease Controls</i>									
16	Disease control (other chronic respiratory conditions), mean age 15 ± 3mo	pg/mL	-	1,434	*362	-	-	-	[39], ns

23	Disease control (other chronic respiratory conditions), uninfected (median age 1.0 yr)	pg/mL	-	471	*107	-	-	-	[26], ns
27	Disease control (other chronic respiratory conditions), infected (median age 1.0 yr)	pg/mL	-	2,114	*421	-	-	-	[26], ns
12	Uninfected control Infants (upper airway obstruction, recurrent or chronic pneumonia, and recurrent or chronic wheezing)	pg/mL	-	*459	-	21 to 2,040	-	-	[34], P
12	Infected control Infants (upper airway obstruction, recurrent or chronic pneumonia, and recurrent or chronic wheezing)	pg/mL	-	*1,860	-	18 to 6,224	-	-	[34], P
12	Uninfected control Infants (upper airway obstruction,	pg/mL (standardised for body mass and BALF)	-	*1,919	-	26 to 10,140	-	-	[34], P

	recurrent or chronic pneumonia, and recurrent or chronic wheezing)	volume)							
12	Infected control Infants (upper airway obstruction, recurrent or chronic pneumonia, and recurrent or chronic wheezing)	pg/mL (standardised for body mass and BALF volume)	-	*4,580	-	37 to 14,687	-	-	[34], P
7	PCD, Mean age 9.2yr	pg/mL	-	*1,272	-	714 to 1,374	-	-	[28], P
26	CRD, Mean age 4.8yr	pg/mL	-	*703	-	31 to 1560	-	-	[28], P
9	Children <6yr with non-CF respiratory conditions	pg/mL	-	55	45	-	-	-	[21], ns
38	6.1±0.6yr Non-CF respiratory conditions	pg/mL	-	716	89.9	-	-	-	[40], P
CF									
31	Infants and young children with CF and no pathogens	Log ₁₀ pg/mL	-	2.3	0.6	-	-	-	[42],P
45	Infants with CF and no pathogens	pg/mL	-	*260	-	-	*128 to 630	-	[23], F, P (2 & 3)
32	Children <6yr with CF and no pathogen	pg/mL	-	427	-	-	269 to 679	-	[21], ns

37	Children <6yr with CF and 10^5 CFU/mL pathogens	pg/mL	-	730	-	-	507 to 1,051	-	[21], ns
15	1.58 (1.12 to 2.9)yr Uninfected, with CF	ng/mL	-	*0.36	-	*0.18 to 1.42	-	-	[9], F (microbiology), P (aliquots 2 & 3)
14	Infants and young children with CF and 10^5 CFU/mL pathogens	pg/mL	-	1,627	-	-	-	-	[22], F
24	Infants and young children with CF and 10^5 CFU/mL pathogens	pg/mL	-	175	-	-	108 to 283	-	[4], svBAL, F
24	Infants and young children with CF and 10^5 CFU/mL pathogens (right middle lobe)	pg/mL	-	229	-	-	114 to 459	-	[4], svBAL, F
39	Infants and young children with CF without infection	μg/mL	-	5.6	-	-	4.0 to 7.9	-	[41], F
IL-6									
<i>Non-CF "Normal" Controls</i>									
10	Infants (congenital stridor)	pg/mL	-	2.1	-	-	0.95 to 4.7	-	[1], F
<i>Non-CF Disease Controls</i>									

12	Infected control Infants (upper airway obstruction, recurrent or chronic pneumonia, and recurrent or chronic wheezing)	pg/mL	-	*71	-	4 to 826	-	-	[34], P
12	Infected control Infants (upper airway obstruction, recurrent or chronic pneumonia, and recurrent or chronic wheezing)	pg/mL (standardised for body mass and BALF volume)	-	*130	-	12 to 1,971	-	-	[34], P
12	Uninfected control Infants (upper airway obstruction, recurrent or chronic pneumonia, and recurrent or chronic wheezing)	pg/mL	-	*10	-	2 to 59	-	-	[34], P
12	Uninfected control Infants (upper airway obstruction, recurrent or chronic pneumonia, and recurrent or chronic wheezing)	pg/mL (standardised for body mass and BALF volume)	-	*25	-	3 to 128	-	-	[34], P

31	Infants and young children with CF and no pathogens	Log ₁₀ pg/mL	-	0.9	0.5	-	-	-	[42], P
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CRD = chronic respiratory disease; PCD = Primary ciliary dyskinesia;

Table E5: Feasibility of BAL				
Participant s	Number (%) of subjects successful	Number of subjects attempted	Reason for exclusion	Author
59 Infants	46 (78%)	59	<5mL BAL fluid obtained	[8], svBAL, F
46 11.3±5.1yr <i>received RhDNase</i>	Time 1: 46 Time 2: 43 Time 3: 24	N/A	Unwillingness to repeat BAL	[2], F, P (2 & 3)
39 12.2±4.4yr <i>no RhDNase</i>	Time 1: 39 Time 2: 33 Time 3: 24	N/A	Unwillingness to repeat BAL	
20 12.5±7.5yr <i>control</i>	Time 1: 20 Time 2: 16 Time 3: 12	N/A	Unwillingness to repeat BAL	

Table E6: Safety of BAL					
Subject type	Additional information	Number of patients (procedures) performed	Number of adverse events (number of patients)	Description of adverse events (n, % of BALs)	Author
CF	≤15mo at study entry	40 (109)	38 events in 26 procedures	Severe (5%): high temperature; severe bronchoconstriction	[21], ns

				Moderate (61%) and Mild (34%): fever, oxygen desaturation, cough or increased secretions	
CF	23.2mo	22	3	Fever (n=3, 14%)	[22], F
CF	Infants and children <6yr	107 (333)	227 events (74% patients)	<p>Fever $\geq 38.5^{\circ}\text{C}$ (n=29, 8.7%)</p> <p>Fever $< 38.5^{\circ}\text{C}$ (n=41, 12.3%)</p> <p>Worsening of cough (n=137)</p> <p>Mild respiratory distress (n=1)</p> <p>Stridor (n=1)</p> <p>Contaminated bronchoscope (n=2)</p>	[43], F
CF	<5yr	-524	282 events	<p>Substantial clinical deterioration within 24h (n=25, 4.8%)</p> <p>Unplanned hospital admission (n=12, 2.3%)</p> <p>Contaminated bronchoscope (n=2, 0.4%)</p> <p>Fever $\geq 38.5^{\circ}\text{C}$ (n=40, 7.6%)</p>	[44], F

				Fever <38.5°C (n=52, 9.9%) Transient worsening of cough (n=151, 29%)	
CF	Median (IQR) 8.5 (5.3 to 11.5)	31 (39)		5 Fever (n=5, 13%)	[45], svBAL, F
CF	20±1(12 to 36)yr FEV1 95 % (60-113)	18		8 No major complications, Fever (n=2, 11%) Mild chest discomfort (n=6, 33%)	[11], P
CF	Adults FEV1 76.0 % (70.0–94.0)	11	(3 patients)	Adverse events in 3 patients, all resulting in prolonged hospitalisation. Hypoxia (n=1) Pyrexia (n=2) WCC + CRP increased (n=1) Shortness of breath (n=1) New changes right mid zone on X-ray (n=1)	[18], F

Right hand column : All samples are BAL unless stated : svBAL = small volume BAL. Aliquot fractions analysed : F = First, P = pooled, ns = not specified.

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