

**Supplemental information**

**The interferon landscape along the respiratory tract impacts the severity of COVID-19**

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		Swab NEG	Swab POS total	Swab POS +	Swab POS ++	Swab POS +++
	<b>Samples (#)</b>	28(183)	155(183)	51(155)	46(155)	58(155)
<b>Age</b>	<b>Minimum</b>	23	10	17	10	26
	<b>Maximum</b>	86	98	93	98	97
	<b>Q1</b>	46	44	46	46	48
	<b>Q3</b>	72	80	83	80	79
	<b>IQR</b>	26	36	37	34	31
	<b>Median</b>	56	58	68	55	61
	<b>Mean</b>	57	60	62	58	62
	<b>≥ 70 (#)</b>	8(28)	61(155)	25(51)	16(46)	20(58)
	<b>&lt; 70 (#)</b>	20(28)	94(155)	26(51)	30(46)	38(58)
	<b>≥ 70 (%)</b>	29	39	49	35	34
<b>&lt; 70 (%)</b>	71	61	51	65	66	
<b>Sex</b>	<b>F (#)</b>	15(28)	85(155)	27(51)	27(46)	31(58)
	<b>M (#)</b>	13(28)	70(155)	24(51)	19(46)	27(58)
	<b>F (%)</b>	54	55	53	59	53
	<b>M (%)</b>	46	45	47	41	47

**SUPPLEMENTAL TABLE 1. Patient information for Swab NEG and Swab POS samples used for gene expression. Related to FIGURE and SUPPLEMENTAL FIGURE 1.** Age, sex and severity characteristics of patient cohorts analyzed in **Figure 1 and Supplemental Figure 1**. Nasopharyngeal swabs from SARS-CoV-2-negative (Swab NEG) and -positive (Swab POS total) subjects, that were further divided in viral load terciles (“Swab POS +”, “Swab POS++”, “Swab POS+++”), were analyzed by qPCR. Q1=quartile 1, Q3=quartile 3, IQR=interquartile range, ≥ 70=over or equal to 70 years old, <70=under 70 years old, F=female, M=male, #=number of samples, %=percentage of samples.

Outcome/gene	Viral load tercile	Age <70		Age ≥70		P value for interaction
		Odds ratio	P value	Odds ratio	P value	
<i>IFNA2</i>	+	Reference(1.0)		Reference(1.0)		0.38
	++	0.7(0.3,2.2)	0.59	0.5(0.1,2.1)	0.36	
	+++	3.2(1.1,9.2)	0.03	0.9(0.2,3.6)	0.89	
<i>IFNA4</i>	+	Reference(1.0)		Reference(1.0)		0.03
	++	1.1(0.2,5.5)	0.92	0.5(0.1,2.4)	0.38	
	+++	10.7(2.4,47.9)	0.002	0.8(0.2,3.0)	0.70	
<i>IFNB1</i>	+	Reference(1.0)		Reference(1.0)		0.14
	++	0.5(0.1,1.5)	0.19	0.5(0.1,1.8)	0.29	
	+++	8.8(2.6,30.2)	<0.001	1.7(0.4,6.8)	0.49	
<i>IFNL1</i>	+	NE		NE		0.06
	++	Reference(1.0)		Reference(1.0)		
	+++	48.0(5.8,399.0)	<0.001	2.1(0.5,8.9)	0.33	
<i>IFNL2,3</i>	+	Reference(1.0)		Reference(1.0)		<0.001
	++	1.0(0.3,3.9)	0.96	0.8(0.2,3.0)	0.80	
	+++	22.1(6.0,82.0)	<0.001	1.0(0.3,3.5)	0.95	
<i>IFNL4</i>	+	Reference(1.0)		Reference(1.0)		0.13
	++	NE		0.6(0.1,3.2)	0.47	
	+++	4.2(1.0,17.6)	0.049	0.6(0.2,2.1)	0.39	
<i>IL1B</i>	+	Reference(1.0)		Reference(1.0)		0.13
	++	5.3(1.6,17.6)	0.005	0.8(0.2,3.6)	0.73	
	+++	11.5(3.1,42.6)	<0.001	NE		
<i>IL6</i>	+	Reference(1.0)		Reference(1.0)		0.80
	++	2.7(0.3,27.8)	0.40	7.8(0.8,79.3)	0.08	
	+++	28.1(3.4,233.1)	0.002	83.90(8.2,857.3)	<0.001	

**SUPPLEMENTAL TABLE 2. Odds ratio of expressing/not each gene across viral load terciles and age groups in swabs from SARS-CoV-2 positive patients. Related to FIGURE SUPPLEMENTAL 1.** Odds ratio of expressing *IFNL1* in “+++” with respect to “++” and *IFNL2,3*, *IFNL4*, *IFNB1*, *IFNA2*, *IFNA4*, *IL1B*, and *IL6* mRNA in “+++” and “++” with respect to “+” swabs from SARS-CoV-2 positive ≥ 70 and < 70 patients was calculated. Odds ratio column indicates the odds ratio and associated 95% confidence interval in brackets. P value column indicates the associated P value for each cohort of patients. Interaction between viral load terciles and age groups (≥70 years vs <70 years) was tested and P values for interaction are indicated. NE=not estimable.

		Gene Expression			Mean Viral RNA CT progression		
		HI	HOSP	ICU	HI	HOSP	ICU
	<b>Samples (#)</b>	9(31)	19(31)	3(31)	6(12)	5(12)	1(12)
<b>Age</b>	<b>Minimum</b>	22	38	60	50	32	NA
	<b>Maximum</b>	78	97	69	84	84	NA
	<b>Q1</b>	42	57	64	54	51	NA
	<b>Q3</b>	51	85	69	73	81	NA
	<b>IQR</b>	9	29	5	19	30	NA
	<b>Median</b>	47	76	68	68	73	91
	<b>Mean</b>	50	71	66	66	64	91
<b>Sex</b>	<b>F (#)</b>	4(9)	9(19)	1(3)	3(6)	2(5)	1(1)
	<b>M (#)</b>	5(9)	10(19)	2(3)	3(6)	3(5)	0(1)
	<b>F (%)</b>	44	47	33	50	40	100
	<b>M (%)</b>	56	53	67	50	60	0

**SUPPLEMENTAL TABLE 3. Patient information for HI, HOSP and ICU Swab samples for gene expression and for Mean Viral RNA CT progression analysis. Related to FIGURE 2 and SUPPLEMENTAL FIGURE 2.** Age, sex and severity characteristics of patient cohorts analyzed in **Figure 2 and Supplemental Figure 2.** Nasopharyngeal swabs from SARS-CoV-2 positive subjects that were either home-isolated (HI), hospitalized (HOSP)) or hospitalized and admitted to the ICU (ICU) were analyzed by qPCR for gene expression or were analyzed longitudinally for mean viral RNA CT. Q1=quartile 1, Q3=quartile 3, IQR=interquartile range, F=female, M=male, #=number of samples, %=percentage of samples.

		Swab NEG	Swab POS
	<b>Samples (#)</b>	3(18)	15(18)
<b>Viral load tercile</b>	<b>+ (#)</b>	NA	3(15)
	<b>++ (#)</b>	NA	6(15)
	<b>+++ (#)</b>	NA	6(15)
<b>Severity</b>	<b>HI (#)</b>	NA	5(15)
	<b>HOSP (#)</b>	NA	7(15)
	<b>ICU (#)</b>	NA	3(15)
<b>Age</b>	<b>Minimum</b>	29	42
	<b>Maximum</b>	86	96
	<b>Q1</b>	51	51
	<b>Q3</b>	80	77
	<b>IQR</b>	29	27
	<b>Median</b>	73	68
	<b>Mean</b>	63	65
<b>Sex</b>	<b>F (#)</b>	1(3)	6(15)
	<b>M (#)</b>	2(3)	9(15)
	<b>F (%)</b>	33	40
	<b>M (%)</b>	67	60

**SUPPLEMENTAL TABLE 4. Patient information for swab samples used for RNA-Seq. Related to FIGURE and SUPPLEMENTAL FIGURE 3.** Age and sex characteristics of patient cohorts analyzed in **Figure 3 and Supplemental Figure 3**. Nasopharyngeal swabs from SARS-CoV-2 positive patients divided in viral load terciles (“+++”, “++”, “+”) and that were either home-isolated (HI), hospitalized (HOSP)) or hospitalized and admitted to the ICU (ICU) were analyzed by RNA-Seq. Q1=quartile 1, Q3=quartile 3, IQR=interquartile range, ≥ 70=over or equal to 70 years old, <70=under 70 years old, F=female, M=male, #=number of samples, %=percentage of samples.

		BALF NEG CTRL	BALF POS	Swab POS
	Samples (#)	24(72)	26(72)	22(72)
Severity	HOSP (#)	NA	5(26)	19(22)
	ICU (#)	NA	21(26)	3(22)
Diagnosis	Fibrosis (#)	8(24)	NA	NA
	Sarcoidosis (#)	8(24)	NA	NA
	Transplant (#)	8(24)	NA	NA
Age	Minimum	33	47	38
	Maximum	100	86	97
	Q1	50	61	58
	Q3	64	71	84
	IQR	14	10	27
	Median	57	66	69.5
	Mean	59	65	70
Sex	F (#)	12(24)	4(26)	12(22)
	M (#)	12(24)	22(26)	10(22)
	F (%)	50	15	55
	M (%)	50	85	45

**SUPPLEMENTAL TABLE 5. Patient information for swab and BALF samples used for gene expression.**

**Related to FIGURE and SUPPLEMENTAL FIGURE 4.** Age and sex characteristics of patient cohorts analyzed in **Figure 4 and Supplemental Figure 4**. Nasopharyngeal swabs and BALF from SARS-CoV-2 positive patients that were either home-isolated (HI), hospitalized (HOSP)) or hospitalized and admitted to the ICU (ICU) and BALF from SARS-CoV-2 negative patients were analyzed by qPCR. Q1=quartile 1, Q3=quartile 3, IQR=interquartile range, , F=female, M=male, #=number of samples, %=percentage of samples.

		BALF NEG CTRL	BALF POS	Swab POS
Viral load tercile	Samples (#)	5(27)	7(27)	15(27)
	+	NA	NA	3(15)
	++	NA	NA	6(15)
	+++	NA	NA	6(15)
Diagnosis	Fibrosis (#)	1(5)	NA	NA
	Sarcoidosis (#)	2(5)	NA	NA
	Transplant (#)	2(5)	NA	NA
Severity	HI (#)	NA	0(7)	5(15)
	HOSP (#)	NA	0(7)	7(15)
	ICU (#)	NA	7(7)	3(15)
Age	Minimum	45	48	42
	Maximum	64	72	96
	Q1	53	66	51
	Q3	63	71	77
	IQR	10	5	27
	Median	63	69	68
	Mean	58	66	65
Sex	F (#)	2(5)	3(7)	6(15)
	M (#)	3(5)	4(7)	9(15)
	F (%)	40	43	40
	M (%)	60	57	60

**SUPPLEMENTAL TABLE 6. Patient information for swab and BALF samples used for RNA-Seq. Related to FIGURE and SUPPLEMENTAL FIGURE 5.** Age and sex characteristics of patient cohorts analyzed in Figure 5 and Supplemental Figure 5. Nasopharyngeal swabs and BALF from SARS-CoV-2 positive patients that were either home-isolated (HI), hospitalized (HOSP)) or hospitalized and admitted to the ICU (ICU) and BALF from SARS-CoV-2 negative patients were analyzed by RNA-Seq. Q1=quartile 1, Q3=quartile 3, IQR=interquartile range, F=female, M=male, #=number of samples, %=percentage of samples.

		COVID-19	ARDS H1N1+	ARDS H1N1-	Fibrosis	Sarcoidosis	Transplant
Age	Samples (#)	29(68)	5(68)	4(68)	10(68)	10(68)	10(68)
	Minimum	28	42	44	64	35	35
	Maximum	79	67	76	83	77	67
	Q1	56	54	54	66	39	53
	Q3	66	62	70	74	53	58
	IQR	10	8	16	8	14	5
	Mean	60	59	63	70	46	56
Sample	Mean	61	57	61	71	50	53
	BALF (#)	29(29)	5(5)	4(4)	10(10)	10(10)	10(10)
	Plasma (#)	17(29)	0(5)	0(4)	0(10)	0(10)	0(10)

**SUPPLEMENTAL TABLE 7. Patient information for BALF and plasma samples used for cytokine quantification. Related to FIGURE and SUPPLEMENTAL FIGURE 6.** Age and type of collected sample of patient cohorts analyzed in **Figure and Supplemental Figure 6**. BALF and plasma from patients with COVID-19 was analyzed. BALF from patients suffering from: non-COVID-19 ARDS (divided in H1N1 Influenza A virus positive or not), fibrosis, sarcoidosis, and that received lung transplant was analyzed. Q1=quartile 1, Q3=quartile 3, IQR=interquartile range.