

**Supplementary Table S1.** Subjects' demographic and clinical characteristics, and investigation of biological samples assigned to each subject. Definition of smoking status: non-smoker=never smoker or not currently smoking and smoked less than 5 pack- year; ex-smoker = not currently smoking and smoked more than 5 pack- year; smoker = currently smoking.

Supplementary Table 1: Clinical Characteristics

Subjects	Age or Age Group	Gender	COVID-19	Smoking History	Clinical Information			Source	Type of Sample			Corresponding Experiments				
					Comorbidities	Clinical Manifestations at Time of Sampling	Ventilator Days		COVID-19 Treatment	HLMVEC (Passage Number)	Lung Tissue Homogenate	Plasma	Lung Tissue (Paraffin-Embedded)	Ceramide Measurements	ECIS	Ceramids
S1	69	F	No	ex-smoker (0.5 pcd x20-25 years)	N/A	ICH, P:F ratio 222	N/A	N/A	NJH	X (P4, 5, 6)				X		
S2	62	F	No	non-smoker	N/A	P:F ratio 310	N/A	N/A	NJH	X (P4, 5)				X		
S3	66	F	No	non-smoker	N/A	N/A	N/A	N/A	NJH	X (P4)				X		
S4	N/A	N/A	No	not available	N/A	N/A	N/A	N/A	Lorca	X (P3, 4, 5, 6)				X		
S5	56	F	No	non-smoker	N/A	P:F ratio 372	N/A	N/A	NJH		X			X		
S6	57	M	No	marijuana 2-3x/week x1 year	N/A	P:F ratio 350	N/A	N/A	NJH		X			X		
S7	52	M	No	non-smoker	N/A	P:F ratio 375	N/A	N/A	NJH		X			X		
S8	24	M	No	non-smoker	N/A	P:F ratio 400	N/A	N/A	NJH		X			X		
S9	31	M	No	1 cigarette/day x1 year	N/A	P:F ratio 491	N/A	N/A	NJH		X			X		
S10	65	F	No	non-smoker	N/A	P:F ratio 470	N/A	N/A	NJH		X			X		
S11	56	M	No	non-smoker	N/A	N/A	N/A	N/A	NJH		X			X		
S12	43	M	No	possible marijuana use	N/A	P:F ratio 435	N/A	N/A	NJH		X			X		
S13	36	F	No	N/A	N/A	N/A	N/A	N/A	NJH		X			X		
S14	56	F	No	N/A	N/A	N/A	N/A	N/A	NJH		X			X		
S15	35	F	No	N/A	N/A	N/A	N/A	N/A	NJH		X			X		
S16	38	F	No	non-smoker	N/A	N/A	N/A	N/A	NJH		X			X		
S17	37	F	No	N/A	N/A	N/A	N/A	N/A	NJH		X			X		
S18	32	F	No	N/A	N/A	N/A	N/A	N/A	NJH		X			X		
S19	56	F	No	N/A	N/A	N/A	N/A	N/A	NJH		X			X		
S20	37	F	No	N/A	N/A	N/A	N/A	N/A	NJH		X			X		
S21	60	F	No	N/A	N/A	N/A	N/A	N/A	NJH		X			X		
S22	35	F	No	N/A	N/A	N/A	N/A	N/A	NJH		X			X		
S23	40	F	No	N/A	N/A	N/A	N/A	N/A	NJH		X			X		
S24	79	F	No	non-smoker	N/A	P:F ratio 572	N/A	N/A	NJH			X			X	
S25	52	M	No	active smoker (30 pack-year)	N/A	P:F ratio 263	N/A	N/A	NJH			X				X
S26	64	M	No	non-smoker	N/A	SAH, P:F ratio 375	N/A	N/A	NJH			X				X
S27	52	M	No	active smoker	HTN, HLD, obesity	N/A	7	N/A	NJH/SJH		X				X	
S28	62	M	No	active smoker	HTN, HLD, obesity	N/A	5	N/A	NJH/SJH		X				X	
S29	61	F	No	ex-smoker (12 pack-year)	N/A	ICH, ARDS from chest trauma, P:F ratio 115, fibrotic ARDS.	N/A	N/A	NJH			X				X
S30	50-59	F	Yes	N/A	asthma, DM	AcRespFall, multiple infections, refractory hypoxia	N/A	HCO <sub>2</sub> , steroids	MSMC		X			X		
S31	30-39	M	Yes	N/A	HTN	AcRespFall, multiple AcRespFall requiring intubation, AKI, AFib, hypotension	N/A	HCO <sub>2</sub> , steroids	MSMC		X			X		
S32	70-79	M	Yes	N/A	HTN, DM, asthma, CKD	AcRespFall, multiple AcRespFall requiring intubation, AKI, AFib, hypotension	N/A	anticoagulation	MSMC		X			X		
S33	70-79	M	Yes	N/A	Parkinson's, HLD, GERD	AFib, bacterial pneumonia	N/A	HCO <sub>2</sub> , anticoagulation	MSMC		X			X		
S34	60-69	M	Yes	N/A	HTN, GERD	AcRespFall with refractory hypoxia and hypotension	N/A	azithromycin, HCO <sub>2</sub>	MSMC		X	X		X		X
S35	60-69	M	Yes	N/A	heart failure, CAD, DM, HTN, HLD, obesity	AcRespFall, gram negative sepsis	N/A	HCO <sub>2</sub> , azithromycin, anticoagulation	MSMC		X	X		X		X
S36	60-69	M	Yes	N/A	HIV, organ transplant, HTN, cancer in remission	AcRespFall, multiple cardiac arrests	N/A	azithromycin, methylprednisolone, anticoagulation	MSMC		X	X		X		X
S37	63	F	Yes	ex-smoker	HTN, trigeminal neuropathy, left bundle branch block, PE	N/A	4	None	NJH/SJH		X			X	X	
S38	64	M	Yes	active smoker	DM, CKD, DVT, depression, hypothyroidism, intellectual disability	N/A	5	convalescent plasma, remdesivir	NJH/SJH		X			X	X	
S39	57	F	Yes	non-smoker	DM, obesity, HTN	N/A	6	convalescent plasma	NJH/SJH		X			X	X	
S40	79	F	Yes	non-smoker	HTN	N/A	3	dexamethasone	NJH/SJH		X			X	X	
S41	69	F	Yes	non-smoker	hypothyroidism, DM, HTN, HLD, PE	N/A	4	none	NJH/SJH		X			X	X	
S42	53	M	Yes	non-smoker	DM, CAD, HTN, hypothyroidism, anxiety, schizophrenia, depression, OCD	N/A	2	HCO <sub>2</sub>	NJH/SJH		X			X	X	
S43	82	F	Yes	ex-smoker	HTN	N/A	1	convalescent plasma, dexamethasone	NJH/SJH		X			X	X	
S44	70	M	Yes	non-smoker	CAD, AICD placement	N/A	2	convalescent plasma, dexamethasone	NJH/SJH		X			X	X	
S45	40	F	Yes	non-smoker	anxiety, hepatitis, pancreatitis, alcohol abuse, essential tremor, depression	N/A	1	none	NJH/SJH		X			X	X	
S46	70	M	Yes	ex-smoker	DM, CKD, HTN, hypothyroidism, dementia	N/A	2	remdesivir	NJH/SJH		X			X	X	
S47	50	M	Yes	non-smoker	obesity	N/A	4	dexamethasone	NJH/SJH		X			X	X	
S48	82	F	Yes	ex-smoker	HTN	N/A	5	convalescent plasma, dexamethasone	NJH/SJH		X			X	X	
S49	56	M	Yes	ex-smoker	obesity, HTN, heart failure, obstructive sleep apnea, hypertriglyceridemia, DM	N/A	6	remdesivir, dexamethasone, convalescent plasma	NJH/SJH		X			X	X	
S50	54	M	Yes	ex-smoker	DM, obesity	N/A	8	remdesivir, dexamethasone, convalescent plasma	NJH/SJH		X			X		
S51	72	M	Yes	ex-smoker	asthma, HTN, HLD	N/A	2	convalescent plasma, remdesivir	NJH/SJH					X	X	
S52	56	M	Yes	non-smoker	DM	N/A	6	dexamethasone, remdesivir, convalescent plasma	NJH/SJH		X			X		
S53	50	M	Yes	non-smoker	obesity	N/A	8	dexamethasone	NJH/SJH		X			X		
S54	62	M	Yes	active smoker	HTN, asthma, stroke, alcohol and illicit substance abuse	N/A	10	none	NJH/SJH		X			X	X	
S55	50-59	F	Yes	N/A	none	died within 2 days of sampling	N/A	none	MSMC		X			X		
S56	60-69	M	Yes	N/A	leukemia in remission, sarcoidosis, DM, HLD, CAD	intubated, requiring pressure, blood and platelet transfusions, cardiac arrhythmias	N/A	enoxaparin, convalescent plasma with transfusion reaction, HCO <sub>2</sub> , steroids	MSMC		X			X		
S57	50-59	M	Yes	N/A	colon cancer	diffuse ground glass opacities, high flow nasal cannula	N/A	convalescent plasma, remdesivir, enoxaparin, methylprednisolone	MSMC		X			X		
S58	30-39	M	Yes	N/A	end stage renal disease on hemodialysis, DM, cardiomyopathy, organ transplant, wound infection	required high flow nasal cannula	N/A	anticoagulation	MSMC		X			X		
S59	20-29	N/A	Yes	N/A	HIV, abscess	asymptomatic COVID	N/A	none	MSMC		X			X		
S60	20-29	F	Yes	N/A	none, in labor	asymptomatic COVID	N/A	none	MSMC		X			X		
S61	60-69	M	Yes	N/A	hyperglycemia, stroke with hemiplegia, cardiac arrest, anoxic brain injury	diffuse ARDS and mild bronchiectasis, ventilator associated pneumonia, died within 2 days of sampling	N/A	none	MSMC		X			X		
S62	68	F	Yes	ex-smoker	GERD, breast cancer, HLD, osteoarthritis, predM, OSA, stress and urinary incontinence	ARDS	4	dexamethasone, remdesivir, convalescent plasma	NJH/SJH		X			X		
S63	66	F	Yes	non-smoker	fibromyalgia	ARDS	6	Regeneron	NJH/SJH		X			X		
S64	54	M	Yes	non-smoker	alcohol abuse	ARDS	6	HCO <sub>2</sub> , methylprednisolone	NJH/SJH		X			X		
S65	89+	F	Yes	N/A	HTN, CKD, GERD	AcRespFall with refractory hypoxia and hypotension	N/A	azithromycin, HCO <sub>2</sub> , steroids, anticoagulation	MSMC		X			X		
S66	80-89	F	Yes	N/A	penicypenia, dementia, HTN	AcRespFall, sepsis with vegetations	N/A	anticoagulation	MSMC		X			X	X	
S67	80-89	F	Yes	N/A	HTN, DM, neurodegenerative disease	AcRespFall	N/A	HCO <sub>2</sub> , anticoagulation	MSMC		X			X	X	
S68	60-69	M	Yes	N/A	HIV, hepatitis C with cirrhosis	AcRespFall	N/A	azithromycin, HCO <sub>2</sub> , anticoagulation	MSMC		X			X		
S69	40-49	M	Yes	N/A	HIV, HTN, asthma	AcRespFall, PE	N/A	azithromycin, HCO <sub>2</sub> , anticoagulation	MSMC		X			X		
S70	50-59	F	Yes	N/A	HTN, CAD, kidney disease	AcRespFall	N/A	azithromycin, HCO <sub>2</sub> , anticoagulation	MSMC		X			X		
S71	40-49	M	Yes	N/A	HIV, HTN, asthma	AcRespFall, PE	N/A	HCO <sub>2</sub> , anticoagulation	MSMC		X			X		X

Abbreviations: F, female; M, male; N/A, not applicable/available; NJH, National Jewish Health Human Lung Tissue Consortium, Denver, CO; SJH, Saint Joseph Hospital, Denver, CO; MSMC, Mount Sinai Medical Center, New York City, NY; X, refers to the type of sample and experiment performed; Blank, not relevant to the subject/sample; pcd, pack per day; HLMVEC, human lung microvascular endothelial cell; P, passage; ECIS, electric cell-substrate impedance sensing; P:F ratio, PaO<sub>2</sub>/FiO<sub>2</sub> ratio; HTN, hypertension; HLD, hyperlipidemia; DM, diabetes mellitus; CAD, coronary artery disease; AKI, acute kidney injury; CKD, chronic kidney disease; OSA, obstructive sleep apnea; HIV, human immunodeficiency virus; DVT, deep vein thrombosis; PE, pulmonary embolism; SAH, subarachnoid hemorrhage; ICH, intracerebral hemorrhage; AFib, atrial fibrillation; AcRespFall, acute hypoxic respiratory failure; ARDS, acute respiratory distress syndrome; HCO<sub>2</sub>, hydrocortisone.

**Supplementary Figure 1. Effect of hydrolyzed COVID-19 patient plasma lipids compared to unmodified COVID-19 patient plasma lipids on human lung microvascular barrier function.** Transcellular electrical resistance (TER) normalized to the time of initial recording ( $\pm$  SEM), measured over time (hours) following addition of unmodified lipids extracted from plasma of COVID-19 patients (COVID PL), COVID PL following alkaline hydrolysis, or vehicle (resuspension buffer).

