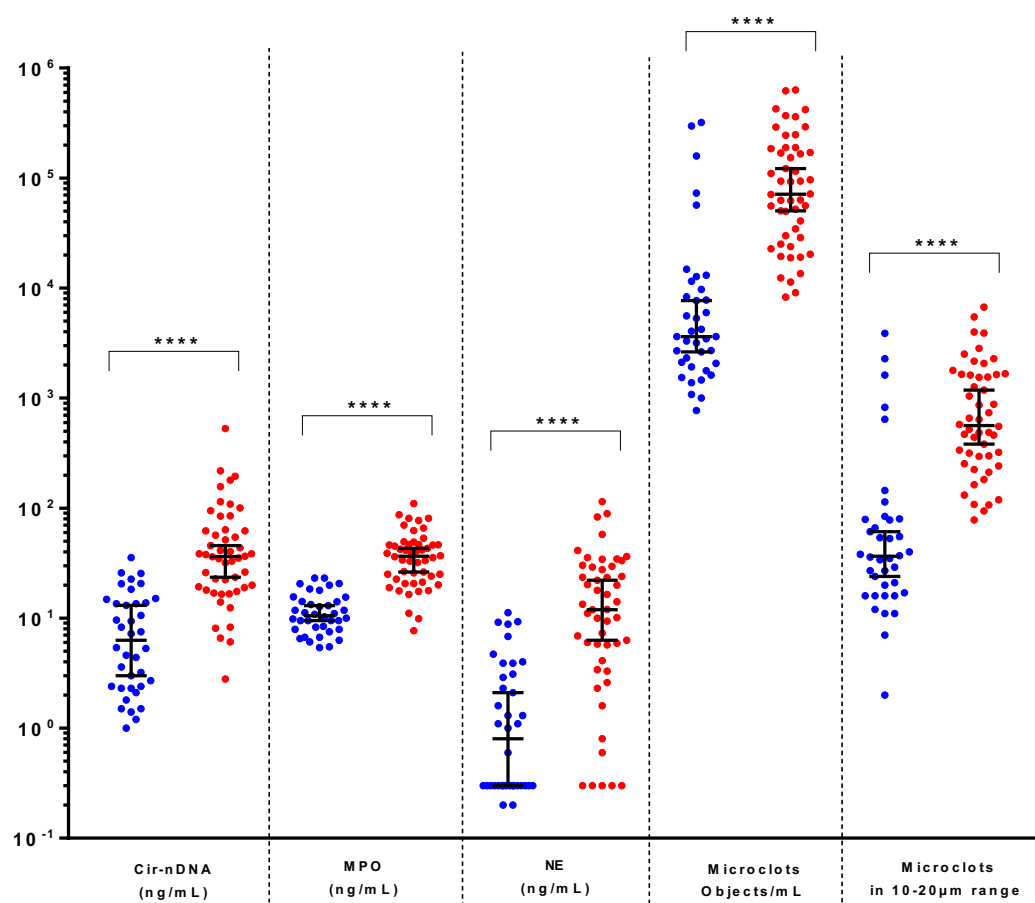
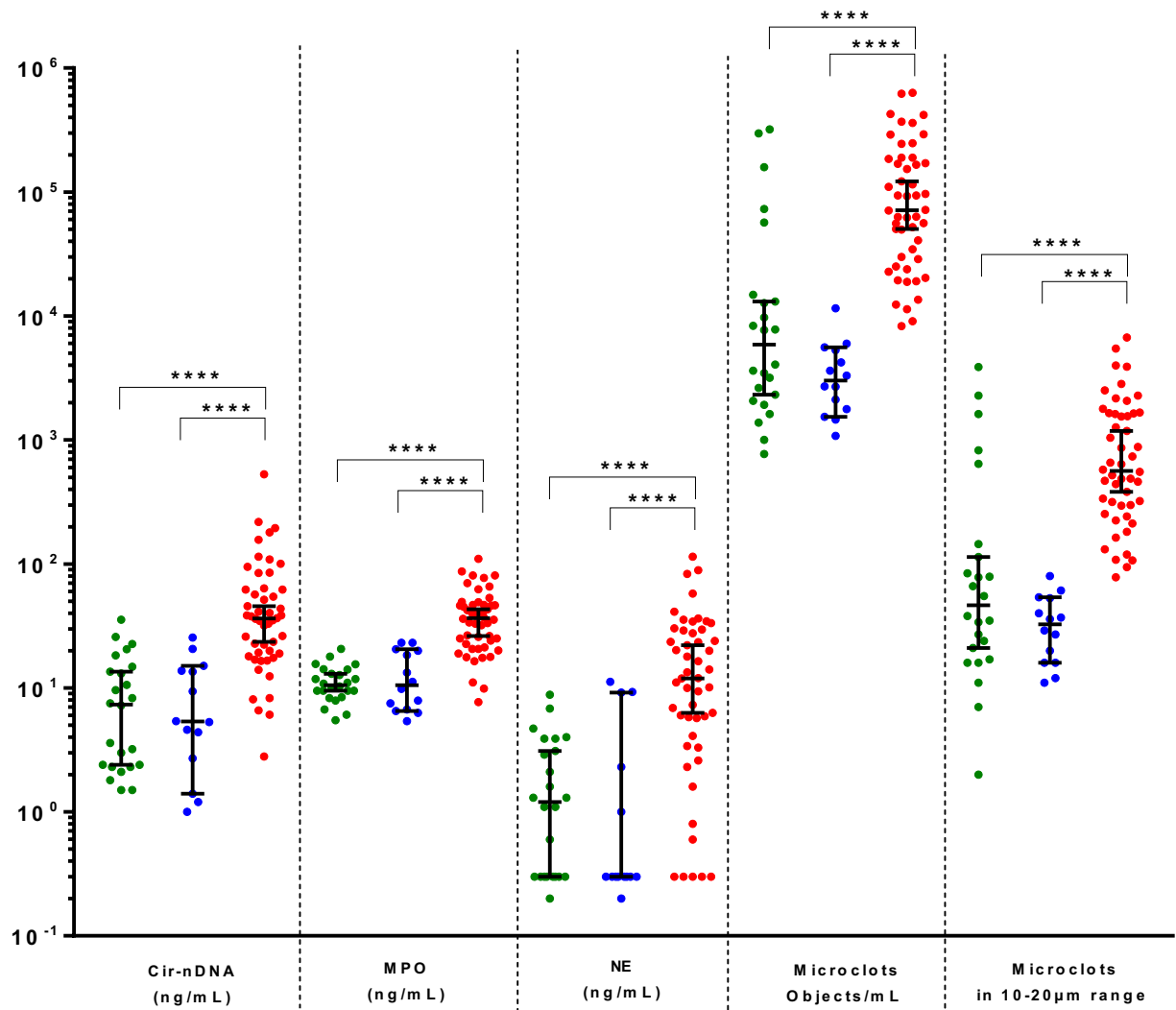


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Median					
Cohorts	Cir-nDNA (ng/mL)	MPO (ng/mL)	NE (ng/mL)	Microclots Objects/mL	Microclots in 10-20 μ m range
(HI EFS + HI SA), n=38	6.3	10.5	0.8	3620.0	36.5
LC, n=50	36.3	36.6	11.9	71394.4	563.5
Fold from median	5.7	3.5	14.9	19.7	15.4

Fig. S1: Values and median of cirDNA, MPO, NE concentration and microclots numbering in plasma of the long COVID (LC) patients and the healthy Individual (HI) cohorts. Healthy individuals (HI) from South Africa (SA) and France (EFS).



Median					
Cohorts	Cir-nDNA (ng/mL)	MPO (ng/mL)	NE (ng/mL)	Microclots Objects/mL	Number of FAM in 10-20µm range
HI EFS, n=24	7.4	10.5	1.2	5885.5	46.5
HI SA, n=14	5.3	10.5	0.3	3008.0	32.5
LC, n=50	36.3	3.6	11.9	71394.4	563.5
Fold (LC/HI EFS) from median	4.9	3.5	9.9	12.1	12.1
Fold (LC/HI SA) from median	6.8	3.5	39.7	23.7	17.3

Fig. S2: Values and median of cirDNA, MPO, NE concentration and microclots numbering in plasma of Long COVID (LC) participants patients and healthy individuals (HI) from France (EFS) and South Africa (SA). Overall, no or poor difference in markers values is noted between SA and EFS HI cohorts.

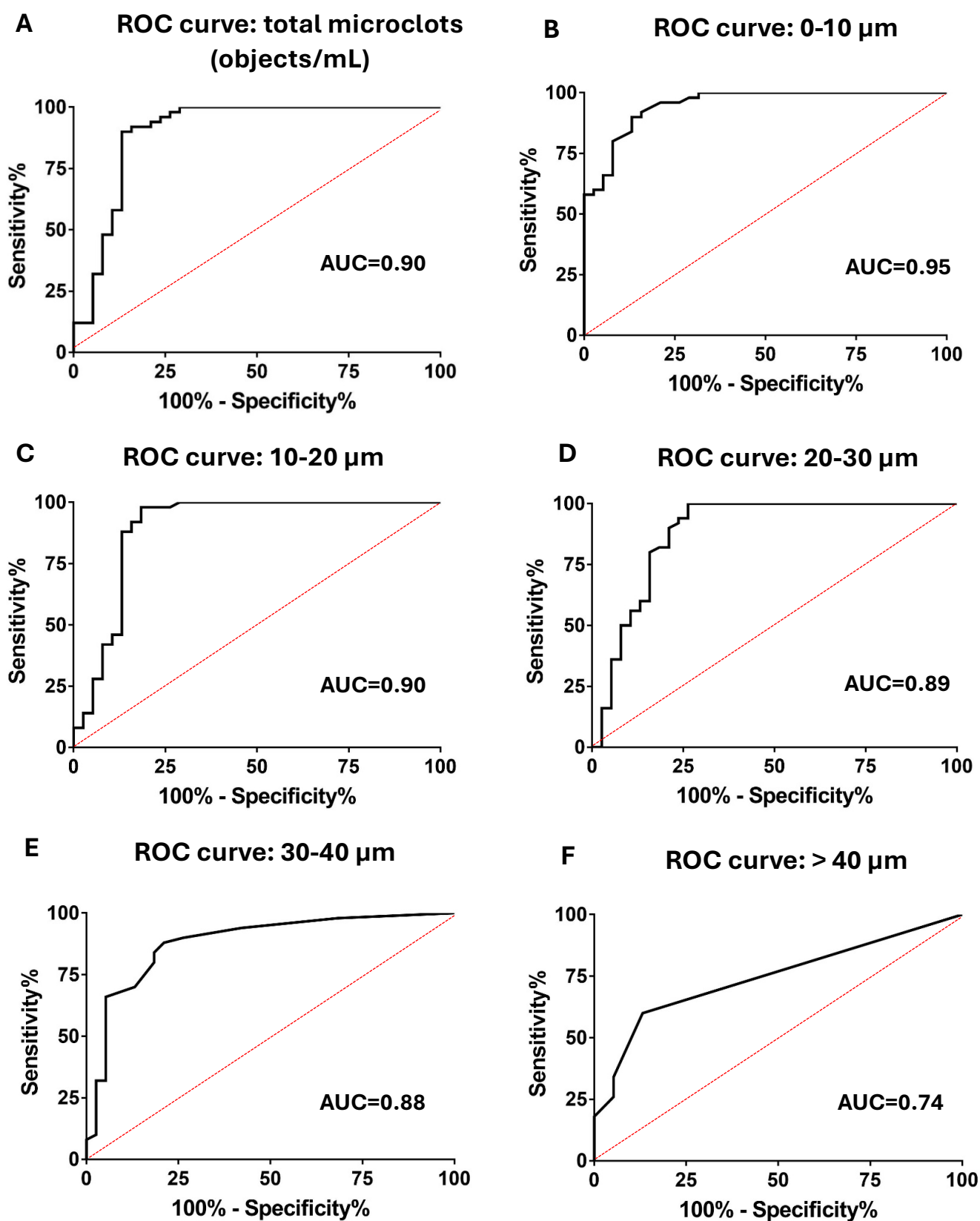


Fig. S3: ROC analysis of microclots numbering vs HI

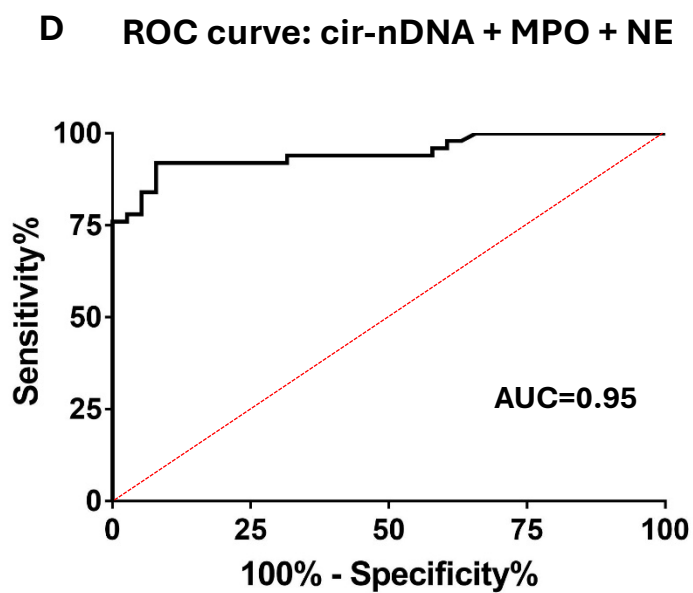
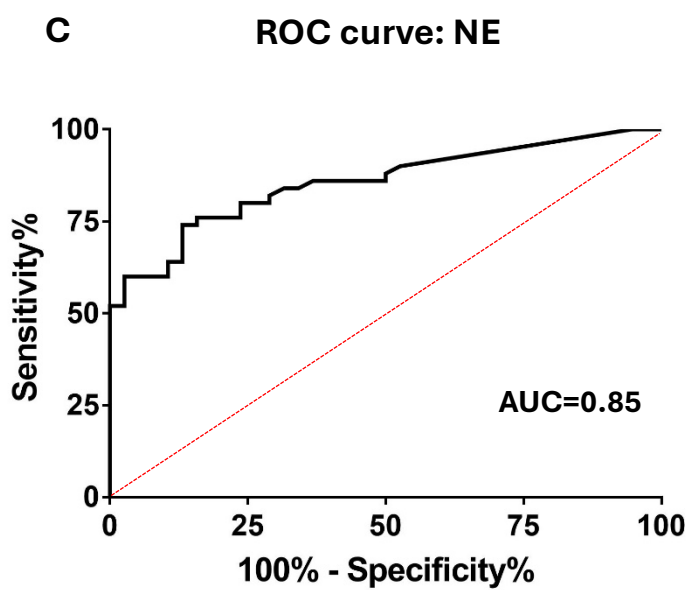
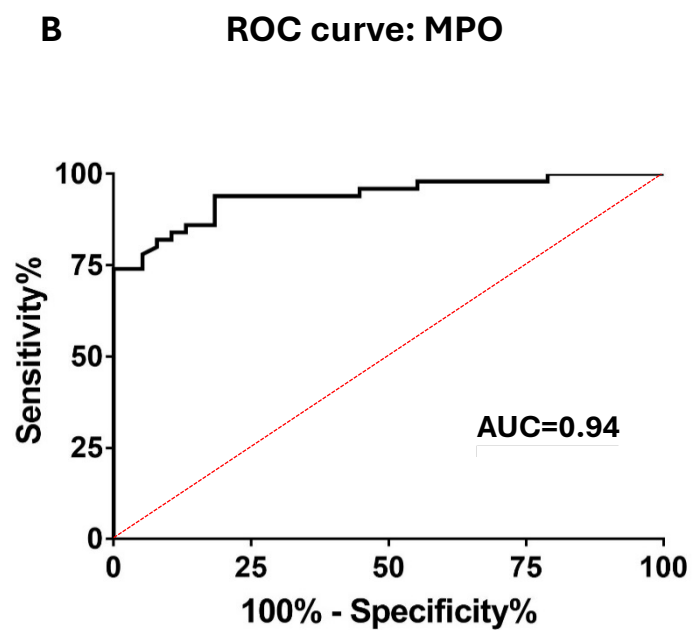
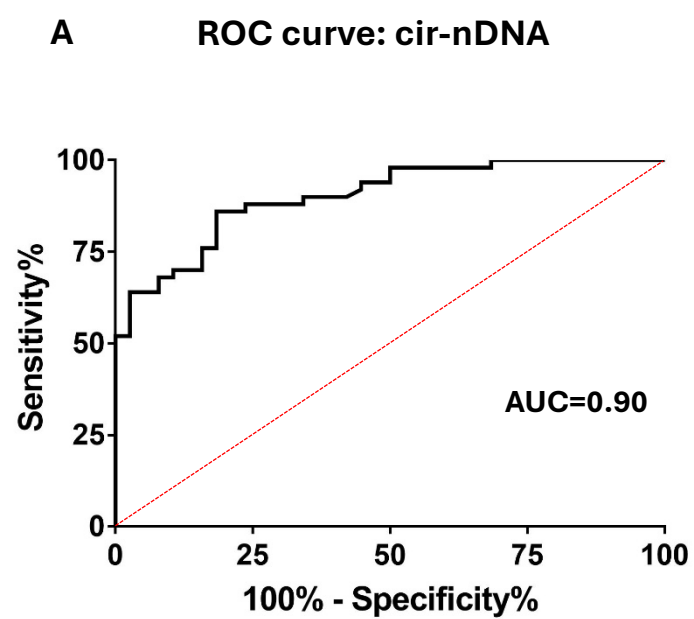


Fig. S4: ROC analysis of cirDNA, MPO, and NE vs Healthy individuals (HI)

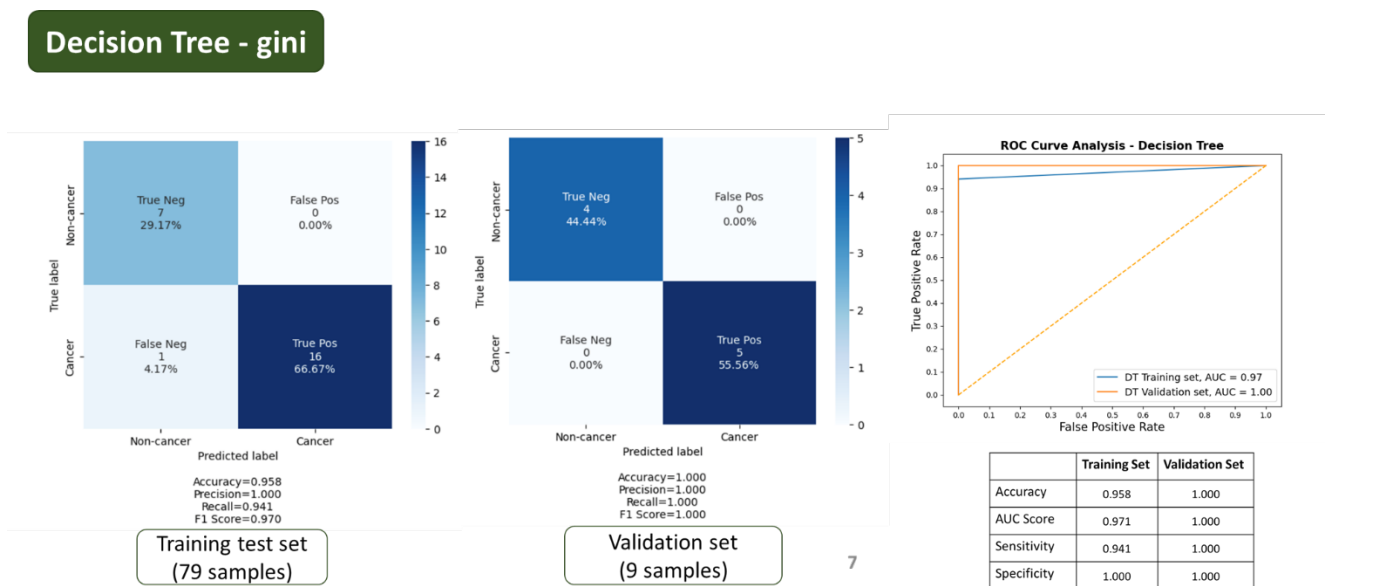
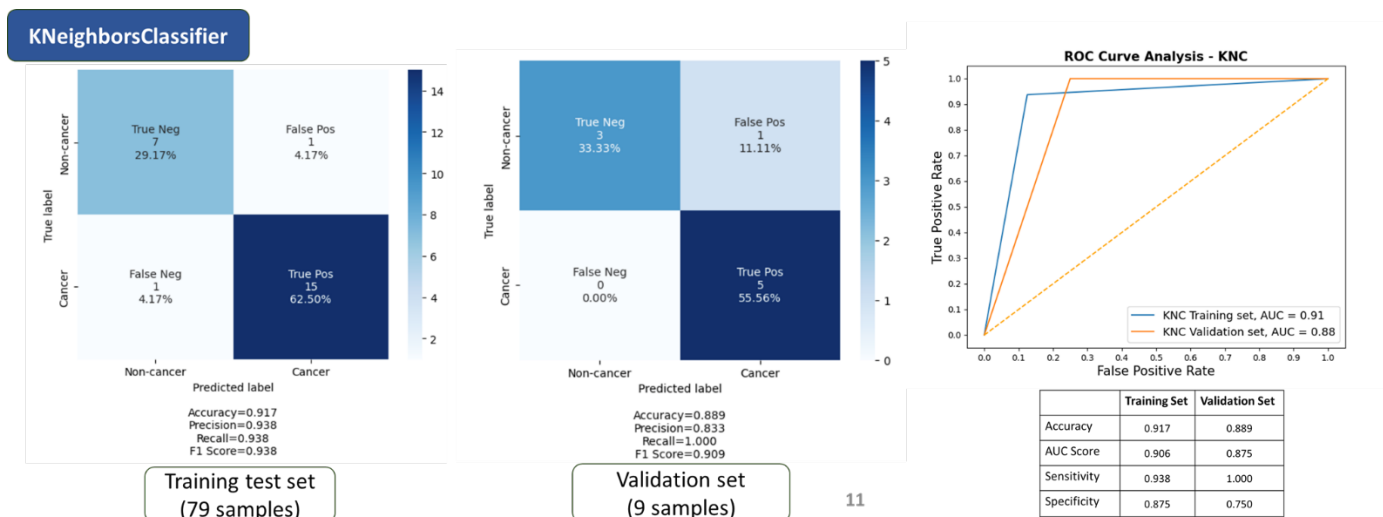
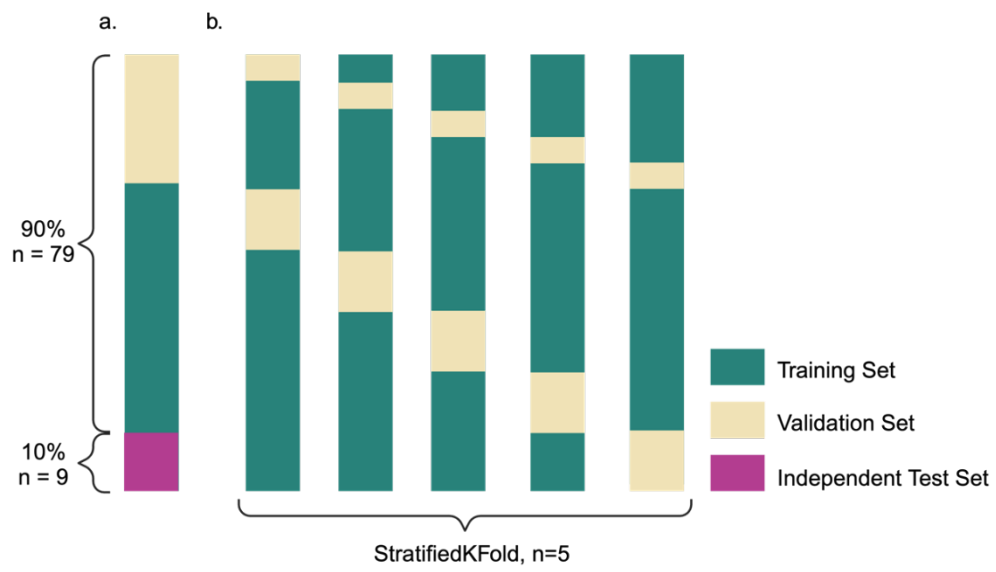


Fig. S5: Data obtained from Kneighbors and Decision Tree – Gini classifiers.



Suppl. Fig. 6. Random Forest stratifiedKfold design on the study cohort. a, and b, without and with stratifiedKfold design, respectively.

Numbers of markers	cir-NDNA	MPO	NE	MC Count	MC 0-10	MC 10-20	MC 20-30	Non Cross-Validation Random Forest Models												Cross-Validation Random Forest Models (Stratified K-Fold)			
								Validation Set (79 samples)				Independent Test Set (9 samples)								Accuracy	AUC	Sensitivity	Specificity
								Accuracy	AUC	Sensitivity	Specificity	Accuracy	AUC	Sensitivity	Specificity	Accuracy	AUC	Sensitivity	Specificity				
7								1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.93	0.93	0.94	0.92				
6								0.96	0.96	0.93	1.00	1.00	1.00	1.00	1.00	0.93	0.93	0.94	0.92				
5								1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.94	0.94	0.94	0.95				
4								1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.94	0.94	0.94	0.95				
3								1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.94	0.94	0.94	0.95				
3								0.92	0.91	0.93	0.90	0.89	0.88	1.00	0.75	0.94	0.94	0.94	0.94				
2								0.96	0.96	0.93	1.00	1.00	1.00	1.00	1.00	0.95	0.95	0.96	0.94				

Fig. S7. Random Forest performances depending on different chosen markers.

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ID Sample	Age	Sex	Group	Rhesus (D)	Hematocrit level
EFS 1	59	M	O	+	50
EFS 2	25	M	O	+	43
EFS 3	64	M	AB	+	48
EFS 4	60	M	A	+	49
EFS 5	63	F	AB	+	40
EFS 6	35	F	O	+	43
EFS 7	35	M	A	+	47
EFS 8	59	M	A	-	43
EFS 9	56	M	A	-	47
EFS 10	37	F	O	+	44
EFS 11	58	F	O	+	38
EFS 12	41	F	A	+	43
EFS 13	61	M	O	+	47
EFS 14	35	M	AB	+	42
EFS 15	37	M	B	+	42
EFS 16	60	F	B	-	47
EFS 17	19	F	O	+	43
EFS 18	49	M	O	+	48
EFS 19	35	F	O	+	44
EFS 20	42	M	O	+	47
EFS 21	32	F	B	-	44
EFS 22	53	M	A	-	47
EFS 23	63	M	O	+	48
EFS 24	25	M	O	+	44

	Cohort of Healthy Individuals (EFS, n=24)		Age	
	Number	(%)	Range	Median
Female (F)	9	37.5%	(19-63)	37
Male (M)	15	62.5%	(25-64)	53

Table S1: Characteristics of the healthy individuals from France (EFS).

Age (represented by median [Q1-Q3])			
Median age of SA healthy individuals (HI, SA) (n = 14)	28 (26-42)		
Median age of French healthy individuals (HI, EFS) (n = 24)	45.5 (35-59.8)		
Median age of Long COVID patients (n = 50)	50 (39-62)		
Sex			
Sex of SA healthy individuals (HI, SA) (n = 14)	7 males; 7 females		
Sex of French healthy individuals (HI, EFS) (n = 24)	15 males; 9 females		
Sex of Long COVID patients (LC) (n = 50)	18 males; 32 females		
Vaccination status of participants before blood collection			
SA healthy individuals (HI, SA) (n = 14)	14 Vaccinated		
French healthy individuals (HI, EFS) (n = 24)	24 Vaccinated		
Long COVID patients (LC) (n = 50)	45 Vaccinated; 4 Unvaccinated; 1 Unknown		
Persistent symptoms in Long COVID (LC) patients (n = 50)			
Symptom	% in 50 Long COVID (LC) patients with symptom		
Brain fog/Concentration issues	78%		
Constant fatigue	74%		
Depression/Anxiety	54%		
Joint and muscle pain	50%		
Sleep apnea	48%		
Shortness of breath	42%		
Heart palpitations	38%		
Digestive problems	32%		
Migraines	24%		
Recurring chest pain	22%		
Vertigo/Dizziness	20%		
Low oxygen levels	18%		
Post-exertional malaise/fatigue	10%		
Parasthesia/numbness	10%		
Tinnitus	6%		
Ageusia (loss of taste)	4%		
Anosmia (loss of smell)	4%		
Kidney complications	2%		
Co-morbidities of Long COVID (LC) patients (n = 50) vs healthy individuals from SA (HI SA, n = 14) vs healthy individuals from EFS (HI EFS, n = 24)			
Co-morbidity	% in 50 Long COVID (LV) Patients	% in 14 SA healthy individuals (HI, SA)	% in 24 EFS healthy individuals (HI, EFS)
Hyperlipidaemia	24%	0%	0%
Hypertension	22%	0%	0%
Gut dysbiosis	10%	0%	0%
Periodontitis or gingivitis	8%	0%	0%
Rheumatoid Arthritis	8%	0%	0%
Cancer	6%	0%	0%
Rosacea	6%	0%	0%
Type 2 Diabetes	6%	0%	0%
Type 1 Diabetes	4%	0%	0%
Cardiovascular disease	4%	0%	0%
Chronic obstructive pulmonary disease	2%	0%	0%

Table S2: Demographics and co-morbidities of our Long COVID (LC) patients and healthy individuals (HI) from both South Africa (SA) and France (EFS).

Median of fibrin amyloid microclots (FAM) parameters as determined by imaging cytofluorometry								
Cohorts	FAM total count	FAM Objects/mL	FAM Mean Area (μm^2)	FAM count in 0-10 μm range	FAM count in 10-20 μm range	FAM count in 20-30 μm range	FAM count in 30-40 μm range	FAM count in > 40 μm range
HI EFS, n=24	76.5	5885.5	289.4	3.0	46.5	11.5	1.5	0.0
HI SA, n=14	39.0	3008.0	207.2	5.0	32.5	2.5	0.5	0.0
(HI EFS + HI SA), n=38	47.0	3620.0	258.5	4.0	36.5	5.0	1.0	0.0
LC, n=50	928.5	71394.4	261.4	97.5	563.5	122.0	14.0	1.0

Table S3: Median of fibrin amyloid microclot (FAM) parameters using cytometry in Long COVID (LC) patients and healthy individuals from both South Africa (SA) and France (EFS).

ID Sample	cirDNA (ng/mL)	MPO (ng/mL)	NE (ng/mL)	FAM total count	FAM Objects/mL	FAM Mean Area (μm^2)	FAM count in 0-10 μm range	FAM count in 10-20 μm range	FAM count in 20-30 μm range	FAM count in 30-40 μm range	FAM count in > 40 μm range
EFS 1	10.6	11.8	1.6	45	3466	285	3	34	6	1	1
EFS 2	14.8	11.0	0.6	25	1925	318	2	17	5	0	1
EFS 3	18.3	12.7	1.1	18	1382	263	3	11	3	1	0
EFS 4	7.5	20.7	2.9	47	3619	207	8	35	3	1	0
EFS 5	13.1	15.5	3.1	4151	320645	233	46	3877	226	2	0
EFS 6	2.3	6.1	1.3	736	56679	283	1	642	90	3	0
EFS 7	2.3	15.6	4.7	170	13092	445	4	84	75	7	0
EFS 8	2.4	14.2	6.8	192	14831	294	11	145	30	6	0
EFS 9	2.4	10.8	0.3	108	8317	439	2	55	44	7	0
EFS 10	9.6	5.5	0.3	165	12707	229	30	114	19	2	0
EFS 11	13.5	7.9	0.3	13	1004	366	1	7	5	0	0
EFS 12	2.1	11.8	0.3	27	2072	299	5	16	6	0	0
EFS 13	3.0	10.0	1.1	2056	158331	324	5	1619	404	25	3
EFS 14	7.2	10.3	4.0	948	72982	267	3	823	115	7	0
EFS 15	8.3	6.7	1.3	3864	297472	408	2	2277	1502	80	3
EFS 16	3.6	17.9	2.1	100	7703	230	10	79	11	0	0
EFS 17	35.5	14.1	8.8	10	770	358	4	2	3	1	0
EFS 18	1.8	9.5	0.2	21	1617	239	3	16	1	1	0
EFS 19	25.8	8.4	0.3	127	9747	414	0	78	43	6	0
EFS 20	22.6	9.5	3.9	41	3167	318	1	27	12	1	0
EFS 21	20.5	13.0	3.9	101	7778	260	19	66	12	4	0
EFS 22	1.5	8.3	0.3	30	2317	257	3	21	5	1	0
EFS 23	1.5	9.5	0.3	34	2626	194	7	24	3	0	0
EFS 24	3.2	9.5	0.3	53	4068	384	3	38	9	2	1
SA 1	1.0	7.9	0.3	150	11551	153	64	80	5	1	0
SA 2	4.6	6.7	0.3	23	1772	337	4	12	5	2	0
SA 3	25.5	20.0	11.2	47	3621	200	5	40	2	0	0
SA 4	2.7	11.2	0.3	29	2115	270	5	20	2	2	0
SA 5	20.6	18.4	9.2	43	3312	186	4	37	2	0	0
SA 6	13.5	23.1	1.0	78	5987	139	17	61	0	0	0
SA 7	15.1	13.3	0.2	73	5603	206	11	53	6	3	0
SA 8	9.4	9.8	0.3	69	5314	203	9	54	4	2	0
SA 9	1.4	20.5	9.3	14	1078	245	1	11	2	0	0
SA 10	13.8	6.3	0.3	55	4236	185	13	36	6	0	0
SA 11	4.4	7.5	0.3	19	1458	215	1	16	2	0	0
SA 12	5.4	6.5	0.3	35	2704	215	2	29	3	1	0
SA 13	1.2	5.4	0.3	35	2686	208	5	27	2	1	0
SA 14	5.3	23.2	2.3	20	1541	235	1	16	3	0	0
HI EFS and HI SA, median (n=38)	6.3	10.5	0.8	47.0	3620.0	258.5	4.0	36.5	5.0	1.0	0.0

Table S4: Compiled data from fibrin amyloid microclot (FAM) parameters, NETs markers and cirDNA in the full healthy cohort. Healthy individuals from both South Africa (SA) and France (EFS)

ID Sample	cirDNA (ng/mL)	MPO (ng/mL)	NE (ng/mL)	FAM total count	FAM Objects/mL	FAM Mean Area (μm^2)	FAM count in 0-10 μm range	FAM count in 10-20 μm range	FAM count in 20-30 μm range	FAM count in 30-40 μm range	FAM count in > 40 μm range
EFS 1	10.6	11.8	1.6	45	3466	285	3	34	6	1	1
EFS 2	14.8	11.0	0.6	25	1925	318	2	17	5	0	1
EFS 3	18.3	12.7	1.1	18	1382	263	3	11	3	1	0
EFS 4	7.5	20.7	2.9	47	3619	207	8	35	3	1	0
EFS 5	13.1	15.5	3.1	4151	320645	233	46	3877	226	2	0
EFS 6	2.3	6.1	1.3	736	56679	283	1	642	90	3	0
EFS 7	2.3	15.6	4.7	170	13092	445	4	84	75	7	0
EFS 8	2.4	14.2	6.8	192	14831	294	11	145	30	6	0
EFS 9	2.4	10.8	0.3	108	8317	439	2	55	44	7	0
EFS 10	9.6	5.5	0.3	165	12707	229	30	114	19	2	0
EFS 11	13.5	7.9	0.3	13	1004	366	1	7	5	0	0
EFS 12	2.1	11.8	0.3	27	2072	299	5	16	6	0	0
EFS 13	3.0	10.0	1.1	2056	158331	324	5	1619	404	25	3
EFS 14	7.2	10.3	4.0	948	72982	267	3	823	115	7	0
EFS 15	8.3	6.7	1.3	3864	297472	408	2	2277	1502	80	3
EFS 16	3.6	17.9	2.1	100	7703	230	10	79	11	0	0
EFS 17	35.5	14.1	8.8	10	770	358	4	2	3	1	0
EFS 18	1.8	9.5	0.2	21	1617	239	3	16	1	1	0
EFS 19	25.8	8.4	0.3	127	9747	414	0	78	43	6	0
EFS 20	22.6	9.5	3.9	41	3167	318	1	27	12	1	0
EFS 21	20.5	13.0	3.9	101	7778	260	19	66	12	4	0
EFS 22	1.5	8.3	0.3	30	2317	257	3	21	5	1	0
EFS 23	1.5	9.5	0.3	34	2626	194	7	24	3	0	0
EFS 24	3.2	9.5	0.3	53	4068	384	3	38	9	2	1
EFS HI median (n=24)	7.4	10.5	1.2	76.5	5885.5	289.4	3.0	46.5	11.5	1.5	0.0

Table S5: Compiled data from fibrin amyloid microclot (FAM) parameters. NETs markers and cirDNA in the healthy individual cohort from France (EFS).

ID sample	cirDNA (ng/mL)	MPO (ng/mL)	NE (ng/mL)	FAM total count	FAM Objects/mL	FAM Mean Area (μm^2)	FAM count in 0-10 μm range	FAM count in 10-20 μm range	FAM count in 20-30 μm range	FAM count in 30-40 μm range	FAM count in > 40 μm range
SA 1	1.0	7.9	0.3	150	11551	153	64	80	5	1	0
SA 2	4.6	6.7	0.3	23	1772	337	4	12	5	2	0
SA 3	25.5	20.0	11.2	47	3621	200	5	40	2	0	0
SA 4	2.7	11.2	0.3	29	2115	270	5	20	2	2	0
SA 5	20.6	18.4	9.2	43	3312	186	4	37	2	0	0
SA 6	13.5	23.1	1.0	78	5987	139	17	61	0	0	0
SA 7	15.1	13.3	0.2	73	5603	206	11	53	6	3	0
SA 8	9.4	9.8	0.3	69	5314	203	9	54	4	2	0
SA 9	1.4	20.5	9.3	14	1078	245	1	11	2	0	0
SA 10	13.8	6.3	0.3	55	4236	185	13	36	6	0	0
SA 11	4.4	7.5	0.3	19	1458	215	1	16	2	0	0
SA 12	5.4	6.5	0.3	35	2704	215	2	29	3	1	0
SA 13	1.2	5.4	0.3	35	2686	208	5	27	2	1	0
SA 14	5.3	23.2	2.3	20	1541	235	1	16	3	0	0
SA HI median (n=14)	5.3	10.5	0.3	39.0	3008.0	207.2	5.0	32.5	2.5	0.5	0.0

Table S6: Compiled data from fibrin amyloid microclot (FAM) parameters, NETs markers and cirDNA in the healthy individual cohort from South Africa (SA).

ID Sample	CirDNA (ng/ml)	MPO (ng/ml)	NE (ng/ml)	FAM total count	FAM Objects/mL	FAM Mean Area (µm²)	FAM count in 0-10µm range	FAM count in 10-20µm range	FAM count in 20-30µm range	FAM count in 30-40µm range	FAM count in > 40µm range
LC1	2.8	11.1	0.3	393	29962	289	16	295	71	11	0
LC2	20	38.8	16.4	8228	631507	271	258	6705	1151	113	1
LC3	37.8	46.4	19.9	1518	114966	266	97	1182	224	14	1
LC4	36.1	36.9	13.4	1443	110014	83	1085	317	39	2	0
LC5	40.2	22.6	6.3	812	62322	202	260	462	80	10	0
LC6	45.6	39.9	6.9	931	71717	336	27	656	218	27	3
LC7	16.9	46.7	27.6	2003	153218	314	45	1552	344	58	4
LC8	217.7	33.3	9.4	2231	171231	324	114	1622	407	79	9
LC9	22.4	40.7	3.3	2203	169082	321	113	1544	470	73	3
LC10	41.2	42.5	11.9	2400	184878	146	1203	1044	140	12	1
LC11	22.8	25.8	5.9	268	20364	247	19	212	34	2	1
LC12	62.1	87.1	41.3	375	28694	261	20	299	46	10	0
LC13	156.7	80.8	114.4	5548	425814	158	2369	2832	326	21	0
LC14	95	65.7	88.8	8297	620169	212	1931	5452	855	59	0
LC15	36.5	45	14.1	741	56120	204	219	441	74	7	0
LC16	179.4	32.1	20.2	3218	247891	279	164	2512	469	69	4
LC17	32.9	35.5	0.6	2150	165620	245	208	1646	276	20	0
LC18	56.7	49.3	35.5	2451	188807	243	325	1779	317	29	1
LC19	38.4	41.7	29.0	824	63051	143	452	321	46	5	0
LC20	85	41.4	12.0	1222	93790	247	154	880	169	17	2
LC21	12.4	77.1	34.6	247	18837	318	20	163	56	7	1
LC22	6.1	62.6	22.1	310	23873	235	33	242	30	5	0
LC23	6.6	9.9	0.3	147	11320	242	11	119	16	1	0
LC24	18	17.7	3.4	656	50349	275	55	489	100	11	1
LC25	8.3	20.1	0.8	248	19034	273	87	107	40	12	2
LC26	51.5	46.7	34.4	3199	244706	287	387	2167	572	69	4
LC27	194.2	33.7	57.7	5445	417909	333	72	3988	1297	81	7
LC28	19	70.1	24.0	537	40805	351	20	381	104	27	5
LC29	16.6	21.2	5.8	161	12357	197	17	131	13	0	0
LC30	34.8	26.2	17.9	836	63106	293	98	552	161	24	1
LC31	14	26.6	5.7	1268	96351	379	32	863	272	90	11
LC32	8.1	7.7	0.3	179	13561	315	29	108	35	6	1
LC33	19.3	17.8	23.5	454	34508	313	11	337	92	14	0
LC34	43.7	53.2	23.4	1584	121982	260	119	1263	181	18	3
LC35	114.2	25.1	0.3	108	8289	282	8	78	20	1	1
LC36	25.9	25.1	6.0	118	9087	254	6	94	15	3	0
LC37	17.5	17.5	10.0	651	49813	245	86	470	89	6	0
LC38	16.5	46.1	10.1	3804	290897	173	1790	1638	327	47	2

LC39	23.6	24.1	2.6	4692	360115	152	2294	2066	307	24	1
LC40	38.5	20.7	4.1	326	25097	262	23	253	44	6	0
LC41	35.1	32.9	33.4	2464	189114	208	546	1668	231	19	0
LC42	26.2	20.6	1.6	1210	92586	426	21	737	357	80	15
LC43	527.5	109.8	83.3	4947	369989	290	170	3908	742	120	7
LV44	109	16.4	0.3	679	52114	200	136	486	51	6	0
LV45	100.5	46.3	11.1	1219	93559	154	566	575	74	4	0
LC46	63.7	80.9	30.2	3810	292421	179	1226	2280	289	15	0
LC47	84.6	36.2	7.3	297	22795	280	12	224	53	6	2
LC48	31.9	43	29.5	253	19353	293	14	182	52	4	1
LC49	62.2	18.9	2.3	727	55798	341	14	521	156	33	3
LC50	54.5	49.5	36.4	926	71071	193	220	640	57	8	1
LC patients median (n=50)	36.3	36.6	11.9	928.5	71394.4	261.4	97.5	563.5	122.0	14.0	1.0

Table S7: Compiled data from fibrin amyloid microclot (FAM) parameters, NETs markers and cirDNA in the long COVID (LC) patient cohort.

Figure 2	Category	p value
A	Total microclots	1.97E-12
	0-10	<0.0000000000000001
	10-20	3.32E-12
	20-30	2.03E-11
	30-40	2.36E-11
	>40	5.33E-06
B	Cirn-DNA	2.01E-12
	MPO	1.00E-15
	NE	1.14E-09

Table S8: P value of the differences between Long COVID (LC) patients and healthy individuals (SA + EFS), in respect to microclot numbers (Figure 2A) and NETs markers and cirDNA (Figure 2B).

	CirDNA (ng/ml)	MPO (ng/ml)	NE (ng/ml)	FAM Objects/mL	FAM count in 0-10µm range	FAM count in 10-20µm range	FAM count in 20-30µm range
Cir-nDNA (ng/ml)							
MPO (ng/ml)	0.186						
NE (ng/ml)	0.086	3.38E-05					
FAM Objects/mL	0.941	0.763	0.324				
FAM count in 0-10µm range	0.943	0.260	0.876	0.017			
FAM count in 10-20µm range	0.979	0.899	0.232	0.00E+00	0.017		
FAM count in 20-30µm range	0.832	0.238	0.453	1.14E-07	0.907	1.60E-06	

Table S9: P values of the significance of the correlation between NETs markers, cirDNA and fibrin amyloid microclots (FAM) in healthy individuals (SA + EFS). 0.00E+00 corresponds to Mann-Whitney P-value with more than 15 decimals.

	CirDNA (ng/ml)	MPO (ng/ml)	NE (ng/ml)	FAM Objects/mL	FAM count in 0-10µm range	FAM count in 10-20µm range	FAM count in 20-30µm range
Cir-nDNA (ng/ml)							
MPO (ng/ml)	0.017						
NE (ng/ml)	0.009	6.65E-12					
FAM Objects/mL	0.002	0.001	0.001				
FAM count in 0-10µm range	0.016	0.003	0.007	1.17E-11			
FAM count in 10-20µm range	0.001	0.003	0.001	0.00E+00	2.26E-08		
FAM count in 20-30µm range	0.015	0.016	0.007	0.00E+00	1.69E-04	0.00E+00	

Table S10: P values of the significance of the correlation between NETs markers, cirDNA and fibrin amyloid microclots (FAM) in patients with long COVID (LC). 0.00E+00 corresponds to Mann-Whitney P-value with more than 15 decimals.

Size Range	Number of individuals with one or more fibrin amyloid microclots (FAM)	
	Healthy Individuals (SA and EFS) (n=38)	Long COVID patients (LC, (n=50))
0-10 µm	37 (97.3%)	50 (100%)
10-20 µm	38 (100%)	50 (100%)
20-30 µm	37 (97.3%)	50 (100%)
30-40 µm	26 (68.4%)	49 (98%)
>40 µm	5 (13.1%)	30 (60%)

Table S11: Number of individuals with one or more fibrin amyloid microclots (FAM) in Long COVID (LC) patients and healthy individuals.