

Supplementary Materials

Supplementary Table S1: Demographic characteristics of all patients.

	Patient class			
	SARS-COV-2 (COVID19)	Infuenza A (INFA)	Respiratory Syncytial Virus (RSV)	Controls
Number	55	55	56	44
Collection year (monthly variation)	2020 (Jan–Apr)	2019–2020 (Dec–Mar)	2019–2020 (Dec–Mar)	2020 (Sept)
Age range	55 years (20–85 years)	62 years (27 days–94 years)	16 months (21 days– 91 years)	24 years (19–43 years)
Sex (%)	M 27% F 42% n/a 31%	M 54% F 44% n/a 2%	M 40% F 46% n/a 14%	M 25% F 75%
Median CTa (range)	26.2 (17.76–37.24)	28.6 (21.43–38.6)	26.3 (18.54–36.87)	N/A

Supplementary Table S2: List of metabolites

Acylcarnitine s			
C0	Carnitine	C10:1	Decenoylcarnitine
C2	Acetylcarnitine	C10	Decanoylcarnitine
C3:1	Propenoylcarnitine	C12:1	Dodecenoylcarnitine
C3	Propionylcarnitine	C12	Dodecanoylcarnitine
C4:1	Butenylcarnitine	C14:2	Tetradecadienylcarnitine
C4	Butyrylcarnitine	C14:1^{1,2}	Tetradecenoylcarnitine
C3OH	Hydroxypropionylcarnitine	C14	Tetradecanoylcarnitine
C5:1 ³	Tiglylcarnitine	C12DC	Dodecanedioylcarnitine
C5	Valeryl carnitine	C14:2OH	Hydroxytetradecadienylcarnitine
C4OH	Hydroxybutyrylcarnitine	C14:1OH	Hydroxytetradecenoylcarnitine
C6:1	Hexenoylcarnitine	C16:2	Hexadecadienylcarnitine
C6	Hexanoylcarnitine	C16:1	Hexadecenoylcarnitine
C5OH	Hydroxyvaleryl carnitine	C16	Hexadecanoylcarnitine
C5:1DC	Glutaconylcarnitin	C16:2OH	Hydroxyhexadecadienylcarnitine
C5DC	Glutaryl carnitine	C16:1OH²	Hydroxyhexadecenoylcarnitine
C8	Octanoylcarnitine	C16OH	Hydroxyhexadecanoylcarnitine
C5MDC	Methylglutaryl carnitine	C18:2	Octadecadienylcarnitine
C9	Nonaylcarnitine	C18:1	Octadecenoylcarnitine
C7DC	Pimelylcarnitine	C18	Octadecanoylcarnitine
C10:2	Decadienylcarnitine	C18:1OH	Hydroxyoctadecenoylcarnitine
Amino Acids			

Ala ^{1,2,3}	Alanine	Lys ^{1,2,3}	Lysine
Arg ^{1,3}	Arginine	Met ^{1,2,3}	Methionine
Asn ^{1,2}	Asparagine	Orn ^{1,2,3}	Ornithine
Asp ^{1,2,3}	Aspartate	Phe ^{1,2,3}	Phenylalanine
Cit ^{1,2}	Citrulline	Pro ^{1,2,3}	Proline
Gln ^{1,2}	Glutamine	Ser ^{1,2,3}	Serine
Glu	Glutamate	Thr ^{1,2,3}	Threonine
Gly ^{1,2,3}	Glycine	Trp	Tryptophan
His ^{1,2,3}	Histidine	Tyr ^{1,2,3}	Tyrosine
Ile ^{1,2,3}	Isoleucine	Val ^{1,2,3}	Valine
Leu ^{1,2}	Leucine		
Benzenoids			
Tyramine Hippuric acid		Homovanillic acid	
Biogenic Amines			
Ac-Orn	Acetylorithine	Met-SO ^{1,2,3}	Methionine sulfoxide
ADMA	Asymmetric dimethylarginine	PEA	Phenylethylamine
alpha-AAA	alpha-Aminoadipic acid	Putrescine ^{1,2,3}	Putrescine
c4-OH-Pro	cis-4-Hydroxyproline	Sarcosine ^{1,2}	Sarcosine
Carnosine ³	Carnosine	Serotonin	Serotonin
Creatinine ^{1,2}	Creatinine	Spermidine ^{1,2}	Spermidine
Dopamine	Dopamine	Spermine ^{1,2}	Spermine
Histamine ^{1,2,3}	Histamine	t4-OH-Pro ^{1,2}	trans-4-Hydroxyproline
Kynurenine ^{1,2,3}	Kynurenine	Taurine ^{1,2}	Taurine
Methylhistidine	Methylhistidine	total DMA ^{1,2}	Dimethylamine
Glycerophospholipids			
LysoPC a C14:0 ^{1,2}	LysoPhosphatidylcholine acyl C14:0	LysoPC a C28:1	LysoPhosphatidylcholine acyl C28:1
LysoPC a C16:1 ^{1,2}	LysoPhosphatidylcholine acyl C16:1	LysoPC a C28:0	LysoPhosphatidylcholine acyl C28:0
LysoPC a C16:0 ^{1,2}	LysoPhosphatidylcholine acyl C16:0	PC aa C32:2	Phosphatidylcholine diacyl C32:2
LysoPC a C17:0 ^{1,2}	LysoPhosphatidylcholine acyl C17:0	PC ae C36:0	Phosphatidylcholine acyl-alkyl C36:0
LysoPC a C18:2 ^{1,2,3}	LysoPhosphatidylcholine acyl C18:2	PC aa C36:6	Phosphatidylcholine diacyl C36:6
LysoPC a C18:1 ^{1,2}	LysoPhosphatidylcholine acyl C18:1	PC aa C36:0	Phosphatidylcholine diacyl C36:0
LysoPC a C18:0 ^{1,2}	LysoPhosphatidylcholine acyl C18:0	PC aa C38:6	Phosphatidylcholine diacyl C38:6
LysoPC a C20:4	LysoPhosphatidylcholine acyl C20:4	Pc aa C38:0	Phosphatidylcholine diacyl C38:0
LysoPC a C20:3 ²	LysoPhosphatidylcholine acyl C20:3	Pc ae C40:6	Phosphatidylcholine acyl-alkyl C40:6
LysoPC a C24:0	LysoPhosphatidylcholine acyl C24:0	PC aa C40:6	Phosphatidylcholine diacyl C40:6
LysoPC a C26:1	LysoPhosphatidylcholine acyl C26:1	PC aa C40:2	Phosphatidylcholine diacyl C40:2
LysoPC a C26:0	LysoPhosphatidylcholine acyl C26:0	PC aa C40:1	Phosphatidylcholine diacyl C40:1
Lipids and lipid-like molecules			
Butyric acid			
Organic acids and derivatives			
Betaine ²		Citric acid ³	
Creatine ²		Succinic acid ³	
Diacetylspermine		Fumaric acid ^{1,2}	
Lactic acid ^{1,2,3}		Pyruvic acid	
beta-Hydroxybutyric acid ^{1,2,3}		Isobutyric acid	
alpha-Ketoglutaric acid		Methylmalonic acid	
DOPA	l-3,4-dihydroxyphenylalanine	Nitro-Tyr	Nitrotyrasine

Propionic acid		p-Hydroxyhippuric acid	para-hydroxyhippuric acid
Organoheterocyclic compounds			
Indole acetic acid		Uric acid ^{1,2}	
Organic nitrogen compounds			
Choline ^{1,2}	Choline	TMAO	Trimethylamine N-oxide
Hexose			
Glucose ³			
Phenylpropanoids and polyketides			
HPHPA		3-(3-Hydroxyphenyl)-3-hydroxypropanoic acid	
Sphingomyelins			
SM(OH) C14:1	Hydroxysphingomyeline C14:1	SM C18:0	Sphingomyeline C18:0
SM C16:1	Sphingomyeline C16:1	SM C20:2	Sphingomyeline C20:2
SM C16:0 ^{1,2,3}	Sphingomyeline C16:0	SM(OH) C22:2	Hydroxysphingomyeline C22:2
SM(OH) C16:1	Hydroxysphingomyeline C16:1	SM(OH) C22:1	Hydroxysphingomyeline C22:1
SM C18:1	Sphingomyeline C18:1	SM(OH) C24:1	Hydroxysphingomyeline C24:1

Supplementary Table S3: Top performed models results for Control Vs RSV.

Initial Results							Stacking Results						
Classifier	Acc	P	R	SP	F1	AUC	Classifier	Acc	P	R	SP	F1	AUC
ExtraTreesClassifier	95.1	95.22	95.1	94.09	95.08	98.94	LinearDiscriminantAnalysis	96.08	96.13	96.08	95.38	96.07	95.92
LGBM	95.1	95.11	95.1	94.63	95.09	98.15	ExtraTrees	96.08	96.33	96.08	94.83	96.05	98.98
LinearDiscriminantAnalysis	94.12	94.12	94.12	93.89	94.12	95.65	RandomForest	96.08	96.33	96.08	94.83	96.05	99
MLPClassifier	93.14	93.13	93.14	92.6	93.13	95.92	AdaBoost	95.1	95.11	95.1	94.63	95.09	94.9
RandomForest	93.14	93.13	93.14	92.6	93.13	98.96	MLPClassifier	94.12	94.15	94.12	94.09	96.78	
SVM	93.14	93.13	93.14	92.6	93.13	94.86	SVM	94.12	94.15	94.12	93.34	94.09	95.18
CatBoost	93.14	93.13	93.14	92.6	93.13	98.86	KNeighbors	94.12	94.34	94.12	92.8	94.08	94.94
KNeighbors	92.16	92.18	92.16	91.31	92.13	94.14	LGBM	94.12	94.12	94.12	93.89	94.12	96.74
XGB	92.16	92.5	92.16	92.95	92.19	93.94	LogisticRegression	93.14	93.13	93.14	92.6	93.13	95.68
AdaBoost	92.16	92.26	92.16	92.4	92.17	94.9	GradientBoosting	93.14	93.13	93.14	92.6	93.13	96.35

Supplementary Table S4: Top performed models results for Control Vs Influenza A.

Initial Results							Stacking Results						
Classifier	Acc	P	R	SP	F1	AUC	Classifier	Acc	P	R	SP	F1	AUC
LinearDiscriminantAnalysis	96.91	96.92	96.9	96.66	96.91	96.09	SVM	97.94	98.01	97.94	97.51	97.93	99.69
SVM	96.91	96.92	96.9	96.66	96.91	95.49	LinearDiscriminantAnalysis	96.91	96.92	96.9	96.66	96.91	96.09
CatBoost	96.91	96.92	96.9	96.66	96.91	99.05	KNeighbors	96.91	97.07	96.91	96.27	96.9	97.66

KNeighborsClassifier	96.91	97.07	96.91	96.27	96.9	97.66	CatBoost	96.91	96.92	96.9	96.66	96.91	99.05
MLPClassifier	95.88	95.88	95.88	95.8	95.88	97.04	MLPClassifier	95.88	95.88	95.88	95.8	95.88	97.04
XGB	95.88	95.94	95.87	95.42	95.87	97.23	LogisticRegression	95.88	95.88	95.88	95.8	95.88	95.75
ElasticNet	95.88	95.88	95.88	95.8	95.88	95.79	XGB	95.88	95.94	95.87	95.42	95.87	97.23
GradientBoosting	94.85	94.99	94.84	94.18	94.82	98.22	ElasticNet_untuned	95.88	95.88	95.88	95.8	95.88	95.79
ExtraTreesClassifier	93.81	93.87	93.82	93.32	93.8	98.67	GradientBoosting	94.85	94.99	94.84	94.18	94.82	98.22
RandomForest	93.81	93.81	93.81	93.71	93.81	98.67	ExtraTrees	93.81	93.87	93.82	93.32	93.8	98.67

Supplementary Table S5: Top performed models results for Control Vs Covid 19.

Initial Results							Stacking Results						
Classifier	Acc	P	R	SP	F1	AUC	Classifier	Acc	P	R	SP	F1	AUC
MLPClassifier	94.95	94.98	94.95	95.05	94.96	96.57	SVM	95.96	96.02	95.96	95.4	95.95	97.23
SVM	94.95	94.96	94.95	94.59	94.94	96.9	LinearDiscriminantAnalysis	94.95	94.96	94.95	94.59	94.94	96.5
AdaBoost	94.95	95.08	94.95	94.14	94.93	95.99	LogisticRegression	94.95	94.96	94.95	94.59	94.94	96.4
RandomForest	94.95	94.96	94.95	94.59	94.94	97.37	AdaBoost	94.95	95.08	94.95	94.14	94.93	96.15
CatBoost	93.94	93.98	93.94	93.33	93.92	98.3	GradientBoosting	94.95	95.08	94.95	94.14	94.93	96.96
LinearDiscriminantAnalysis	93.94	93.98	93.94	93.33	93.92	96.36	ElasticNet	94.95	94.96	94.95	94.59	94.94	96.44
LogisticRegression	92.93	92.96	92.93	92.98	92.94	96.61	MLPClassifier	93.94	93.94	93.94	93.79	93.94	95.57
ExtraTrees	92.93	92.96	92.93	92.98	92.94	97.25	CatBoost	93.94	93.98	93.94	93.33	93.92	98.26
LGBM	92.93	92.96	92.93	92.98	92.94	96.77	RandomForest	92.93	92.93	92.93	92.53	92.92	97.47
ElasticNet	92.93	92.96	92.93	92.98	92.94	96.61	ExtraTrees	92.93	92.93	92.93	92.53	92.92	96.52

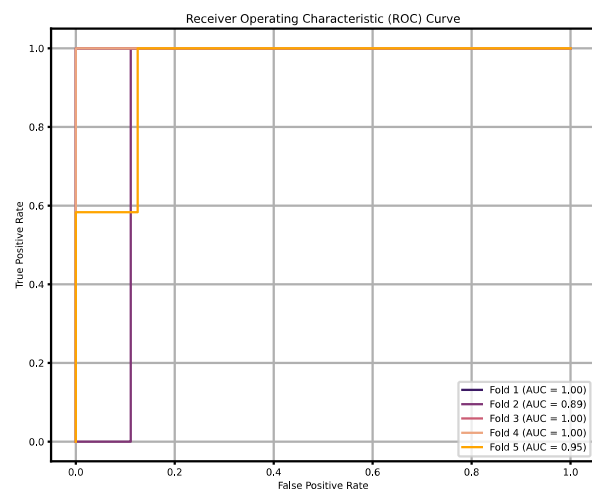
Supplementary Table S6: Top performed models results for Control Vs All Respiratory Virus.

Initial Results							Stacking Results						
Classifier	Acc	P	R	SP	F1	AUC	Classifier	Acc	P	R	SP	F1	AUC
CatBoost	97.14	97.14	97.14	94.23	97.14	99.17	RandomForest	98.1	98.09	98.1	94.48	98.08	97.78
ExtraTrees	97.14	97.12	97.15	92.56	97.12	98.8	ExtraTrees	97.62	97.6	97.62	94.36	97.61	99.04
MLPClassifier	96.67	96.7	96.67	94.1	96.68	95.65	XGB	97.62	97.62	97.62	92.69	97.59	99.72
AdaBoost	96.67	96.8	96.67	95.77	96.7	96.71	MLPClassifier	97.14	97.14	97.14	94.23	97.14	97.04
RandomForest	96.67	96.64	96.66	92.44	96.65	98.8	LogisticRegression	97.14	97.14	97.14	94.23	97.14	98.12
LogisticRegression	96.19	96.28	96.19	93.98	96.22	96.13	KNeighbors	97.14	97.14	97.14	94.23	97.14	96.12
SVM	96.19	96.19	96.19	92.31	96.19	96.26	AdaBoost	97.14	97.14	97.14	94.23	97.14	94.42

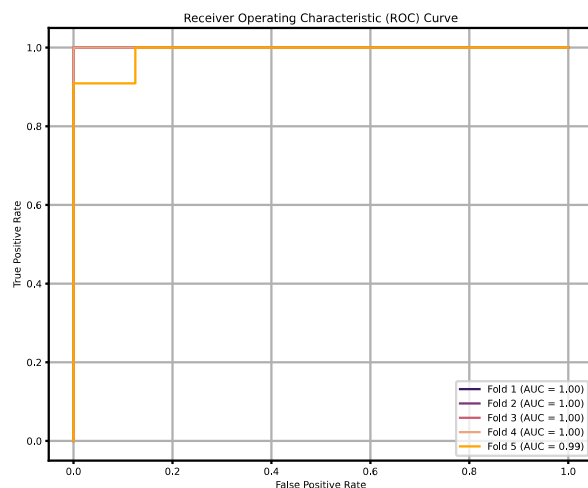
KNeighbors	95.24	95.48	95.24	93.72	95.31	95.23	SVM	97.14	97.14	97.14	94.23	97.14	93.09
LGBM	95.24	95.24	95.24	90.39	95.24	98.41	ElasticNet	97.14	97.14	97.14	94.23	97.14	98.22
ElasticNet	95.24	95.48	95.24	93.72	95.31	96.15	CatBoost	96.67	96.64	96.67	90.77	96.62	98.64

Supplementary Table S7: Top performed models results for COVID-19 vs influenza A/RSV

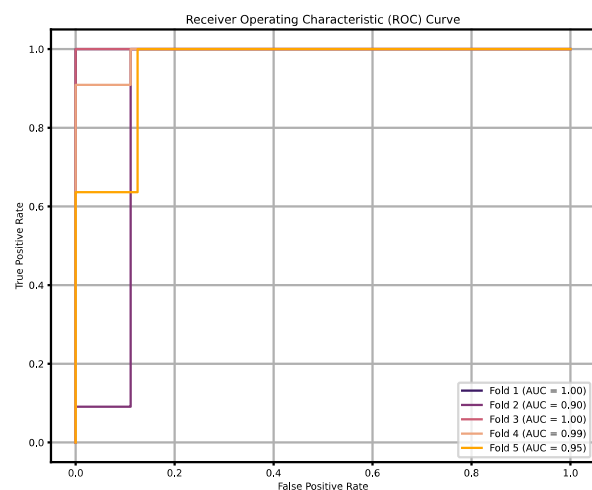
Initial Results							Stacking Results						
Classifier	Acc	P	R	SP	F1	AUC	Classifier	Acc	P	R	SP	F1	AUC
ExtraTrees	83.73	83.49	83.74	77.26	83.53	88.15	LogisticRegression	86.14	85.97	86.14	80.3	85.97	87.68
LogisticRegression	83.73	84	83.74	80.93	83.84	88.2	ElasticNet	86.14	85.97	86.14	80.3	85.97	87.68
ElasticNet	83.73	84	83.74	80.93	83.84	88.23	SVM	85.54	85.36	85.54	80	85.4	87.02
RandomForest	83.13	83	83.13	77.89	83.05	87.82	ExtraTrees	85.54	85.45	85.54	77.24	85.13	84.95
LinearDiscriminantAnalysis	82.53	82.61	82.53	78.51	82.57	85.2	KNeighbors	85.54	85.45	85.54	77.24	85.13	82.61
CatBoost	81.93	81.67	81.93	75.45	81.75	87.73	CatBoost	84.94	85.02	84.94	75.1	84.34	84.14
SVM	81.93	82.11	81.93	78.21	82.01	87.92	MLPClassifier	84.34	84.1	84.34	76.64	83.99	83.78
KNeighbors	80.72	81.69	80.72	79.44	81.02	82.07	RandomForest	84.34	84.1	84.34	76.64	83.99	82.13
LGBM	79.52	79.51	79.51	74.26	79.51	86.13	XGB	83.13	82.96	83.13	73.3	82.53	82.08
MLPClassifier	78.31	77.77	78.32	69.08	77.84	80.62	LinearDiscriminant Analysis	82.53	82.33	82.53	76.67	82.4	85.15



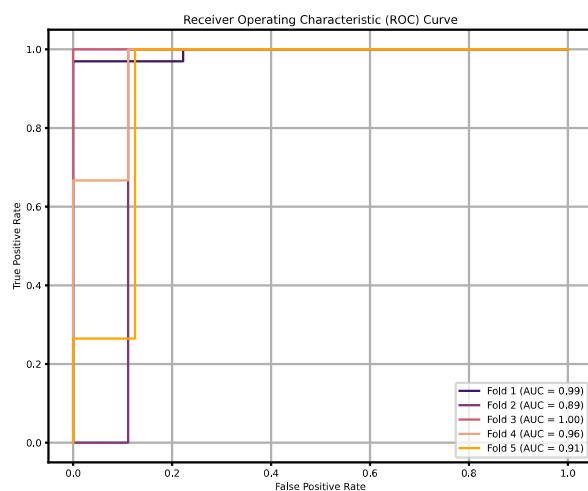
(A)



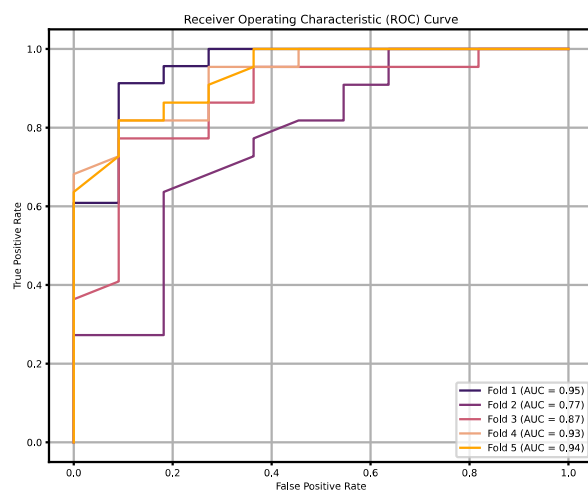
(B)



(C)

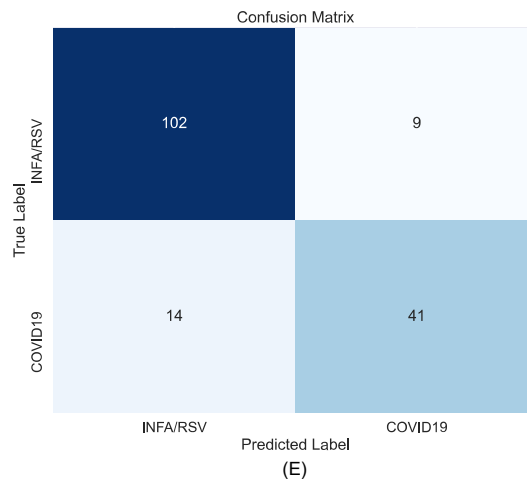
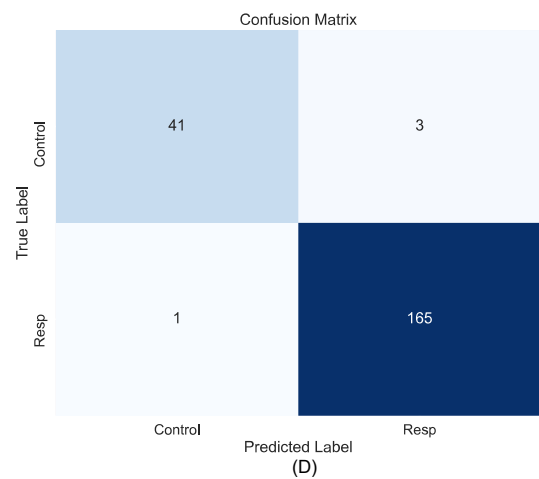
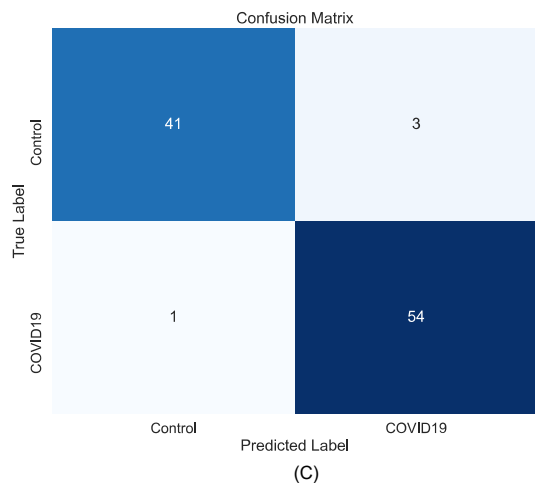
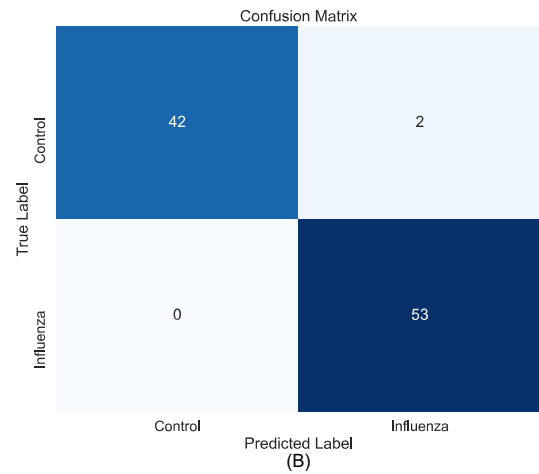
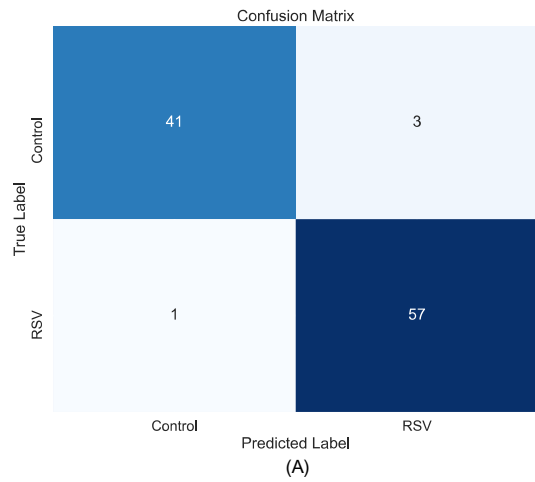


(D)



(E)

Supplementary Figure S1: AUC curve for different cases (A) Control Covid 19 Vs (Influenza A/RSV)Vs RSV (B) Control Vs Influenza A (C) Control Vs Covid 19 (D) Control Vs All Respiratory Virus (E) Covid 19 Vs (Influenza A/RSV).



Supplementary Figure S2: Confusion Matrix curve for different cases (A) Control Covid 19 Vs (Influenza A/RSV)Vs RSV (B) Control Vs Influenza A (C) Control Vs Covid 19 (D) Control Vs All Respiratory Virus (E)) Covid 19 Vs (Influenza A/RSV).