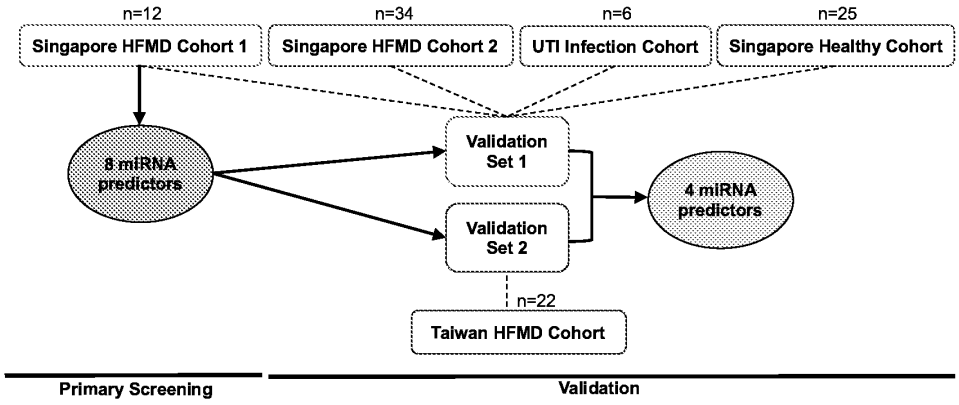
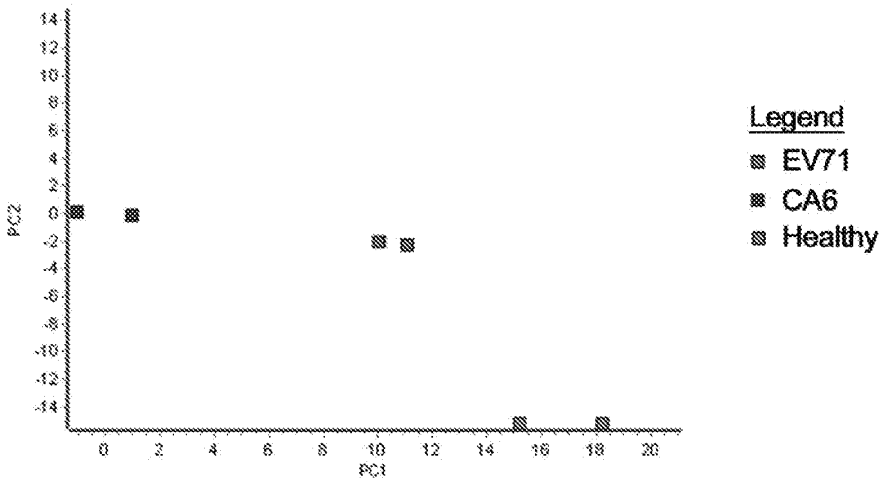

n=12
n=34
n=6
n=25
Singapore HFMD Cohort 1
Singapore HFMD Cohort 2
UTI Infection Cohort
Singapore Healthy Cohort
8 miRNA predictors
Validation Set 1
Validation Set 2
4 miRNA predictors
n=22
Taiwan HFMD Cohort
Primary Screening
Validation

Figure 1

A


PC2
PC1
Legend
EV71
CA6
Healthy

B

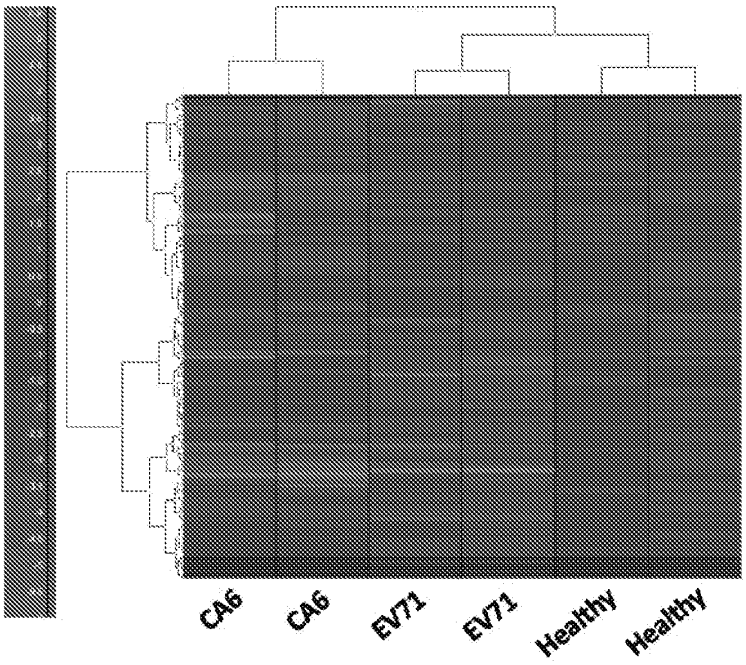

CA6
CA6
EV71
EV71
Healthy
Healthy

Figure 2

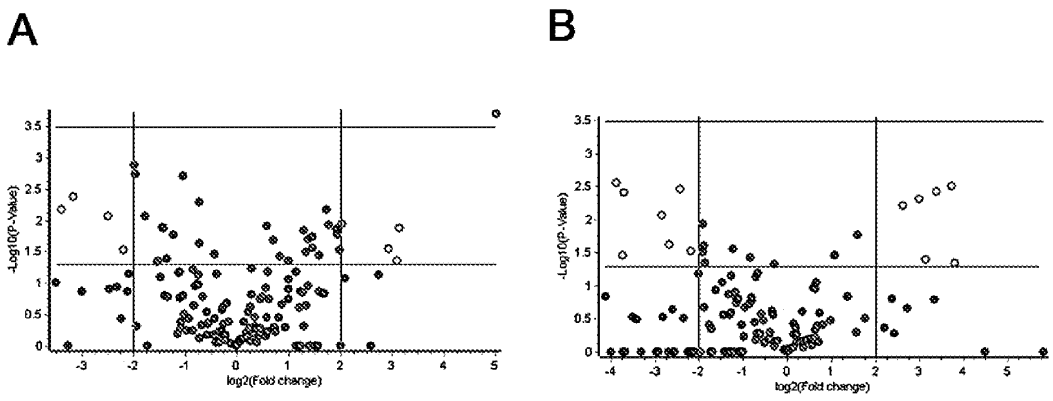


Figure 3

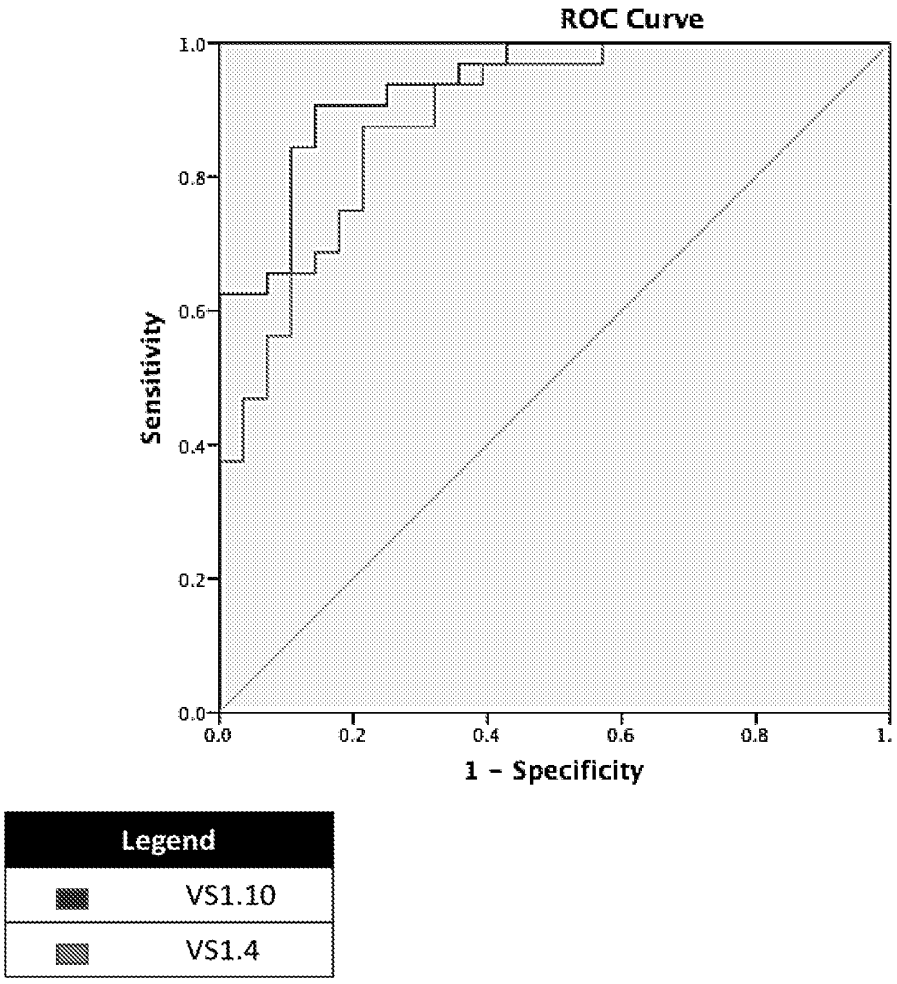

ROC Curve
Sensitivity
1 – Specificity
1.0
0.8
0.6
0.4
0.2
0.0
0.0
0.2
0.4
0.6
0.8
Legend
VS1.10
VS1.4

Figure 4

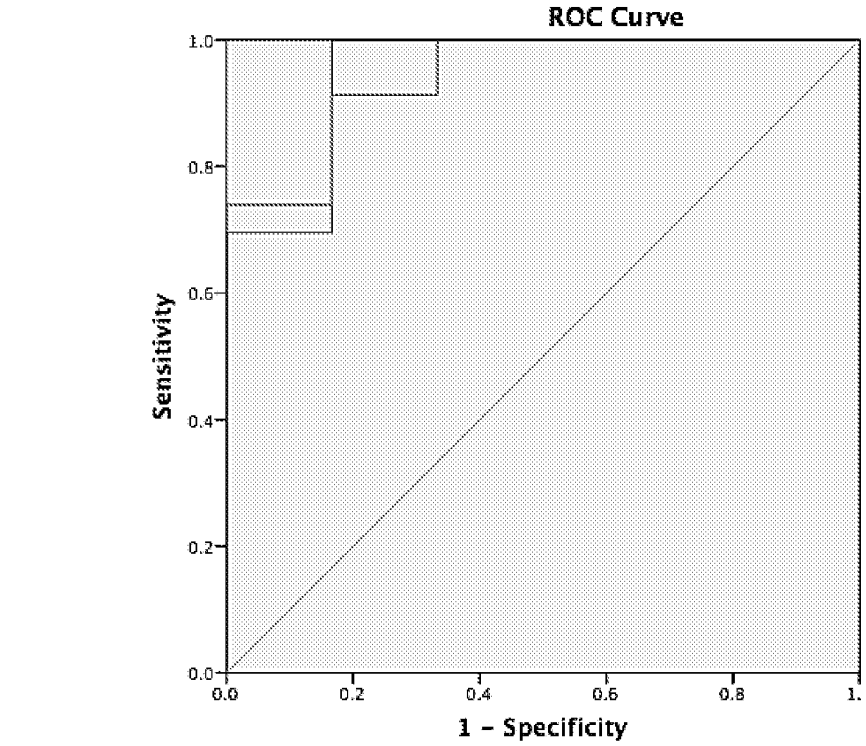

ROC Curve
Sensitivity
1 – Specificity
0.0
0.2
0.4
0.6
0.8
1.0
Legend
VS2.10
VS2.4

Figure 5

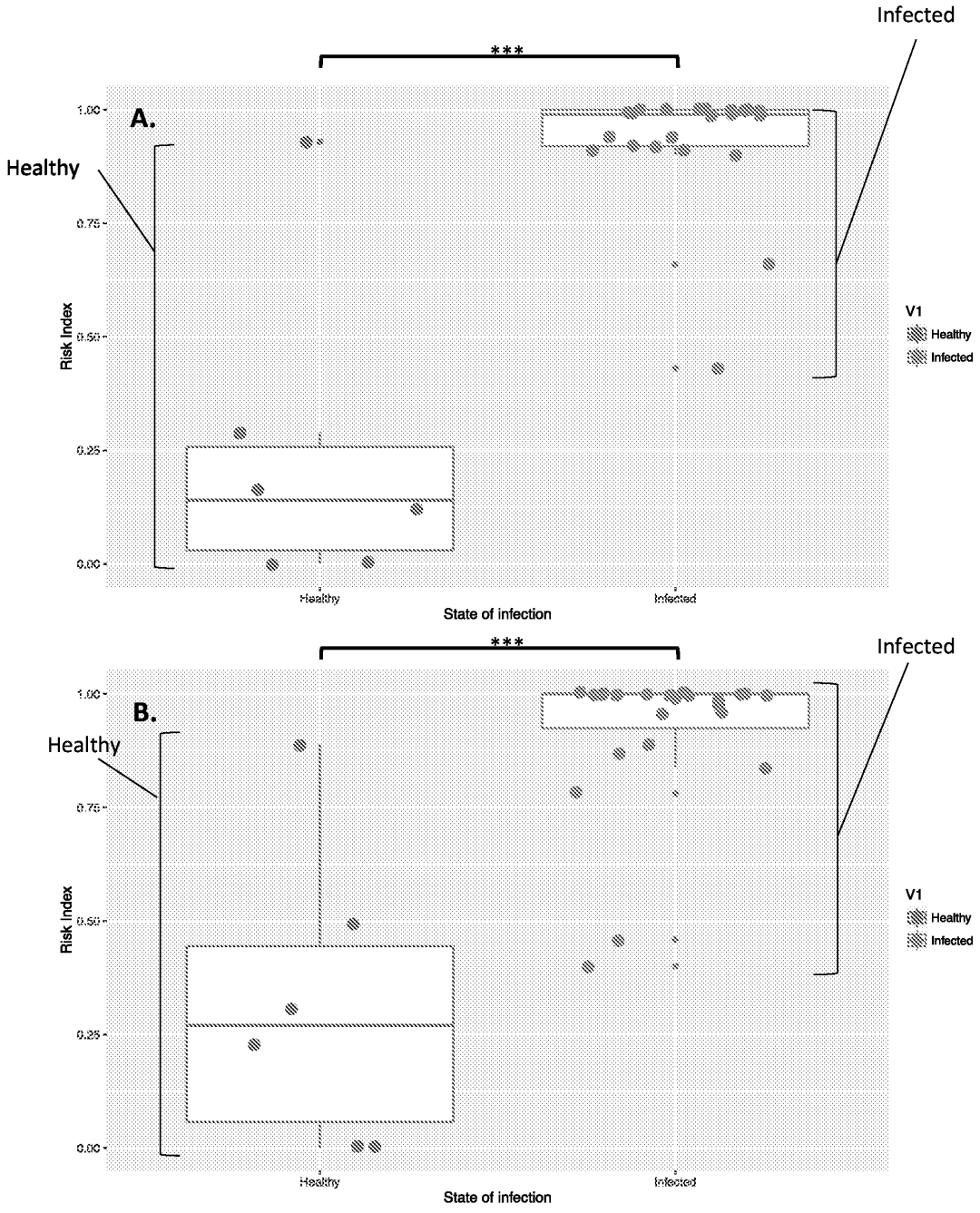

A.
***
Infected
Healthy
1.00
0.75
0.50
0.25
0.00
Risk Index
Healthy
Infected
State of infection
V1
Healthy
Infected
B.
***
Infected
Healthy
1.00
0.75
0.50
0.25
0.00
Risk Index
Healthy
Infected
State of infection
V1
Healthy
Infected

Figure 6

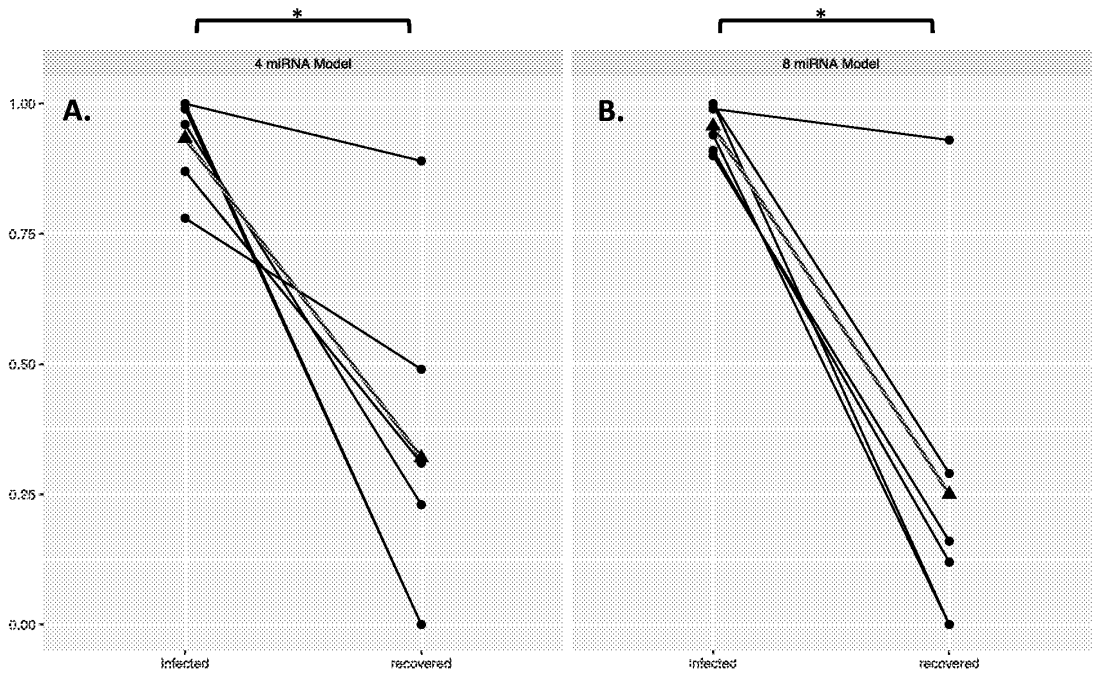

*
4 miRNA Model
A.
1.00
0.75
0.50
0.25
0.00
infected
recovered
*
8 miRNA Model
B.
infected
recovered

Figure 7

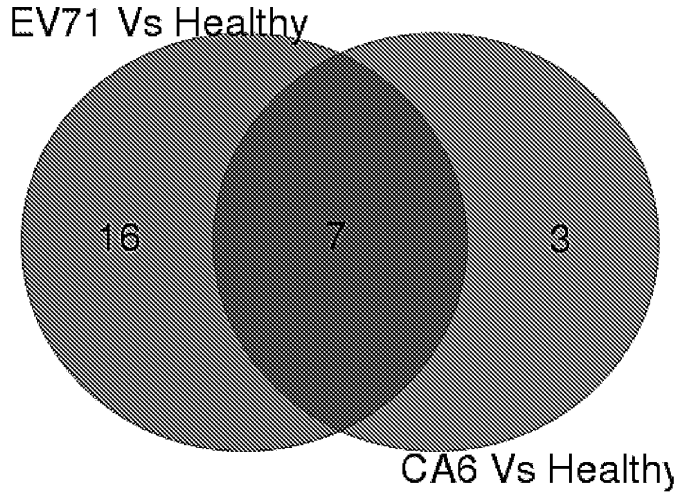


Figure 8

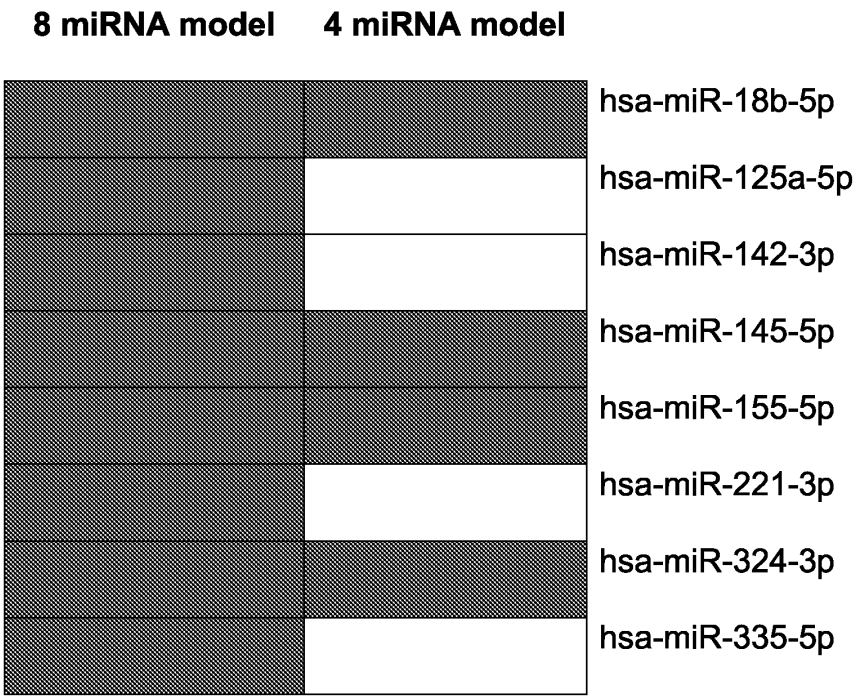

8 miRNA model
4 miRNA model
hsa-miR-18b-5p
hsa-miR-125a-5p
hsa-miR-142-3p
hsa-miR-145-5p
hsa-miR-155-5p
hsa-miR-221-3p
hsa-miR-324-3p
hsa-miR-335-5p

Figure 9

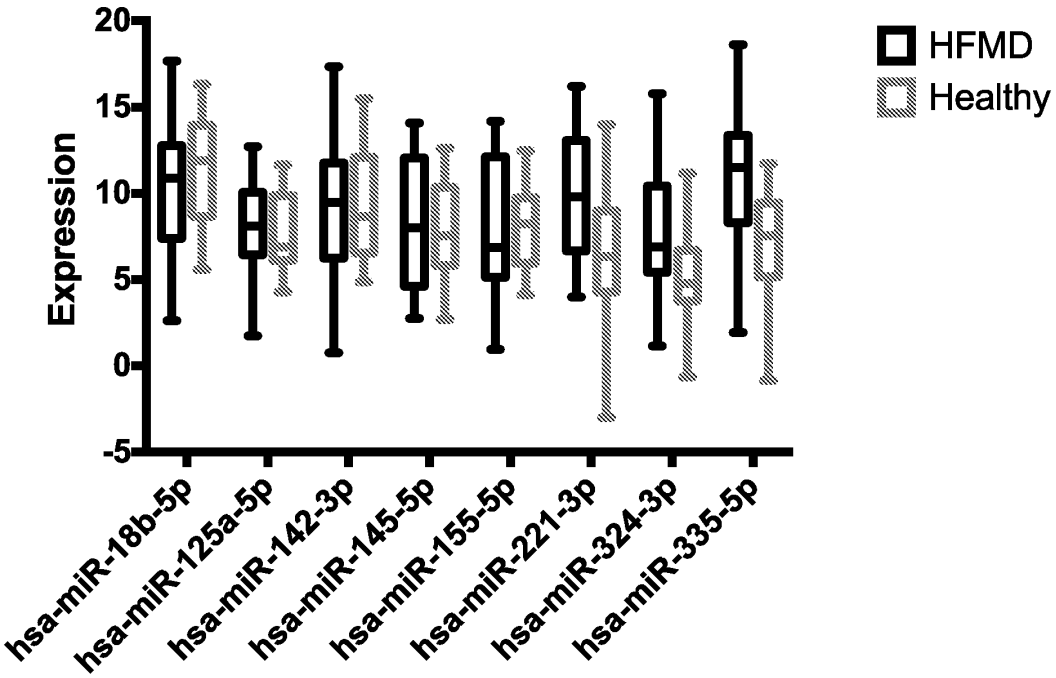

20
15
10
5
0
-5
Expression
HFMD
Healthy
hsa-miR-18b-5p
hsa-miR-125a-5p
hsa-miR-142-3p
hsa-miR-145-5p
hsa-miR-155-5p
hsa-miR-221-3p
hsa-miR-324-3p
hsa-miR-335-5p

Figure 10

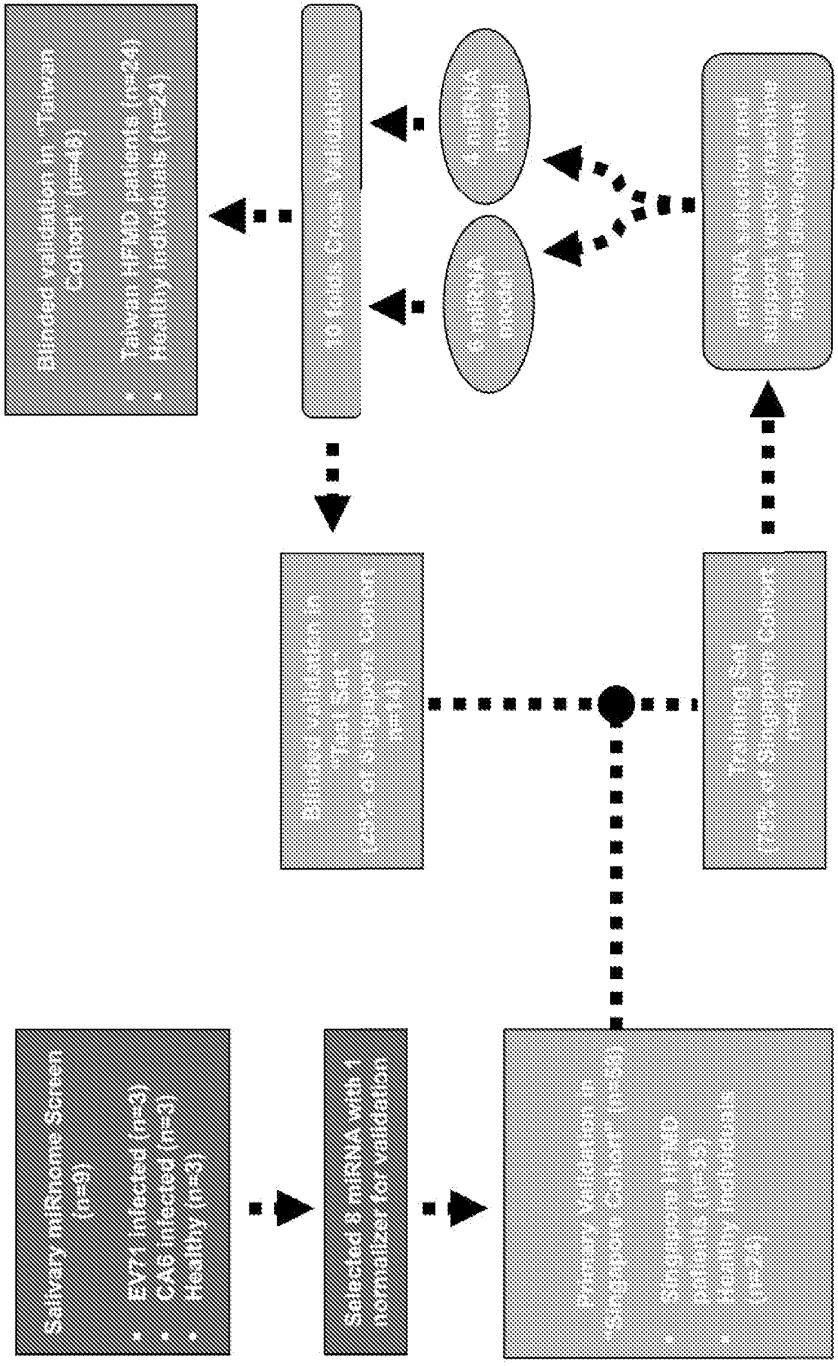

Blinded Validation in Taiwan
Cohort 1 (n=46)
Taiwan HPAH patients (n=24)
Healthy individuals (n=22)
10 Gene Signature Validation
Training Cohort
Validation Cohort
Blinded Validation in Singapore Cohort (n=40)
Training Cohort (n=40)
Validation Cohort (n=40)
Selected 3 miRNA with 1 normalizer for Validation
Serum/Plasma miRNA Levels
Healthy (n=0)
COPD patients (n=0)
IPAH patients (n=0)
SSc-PAH patients (n=0)

Figure 11

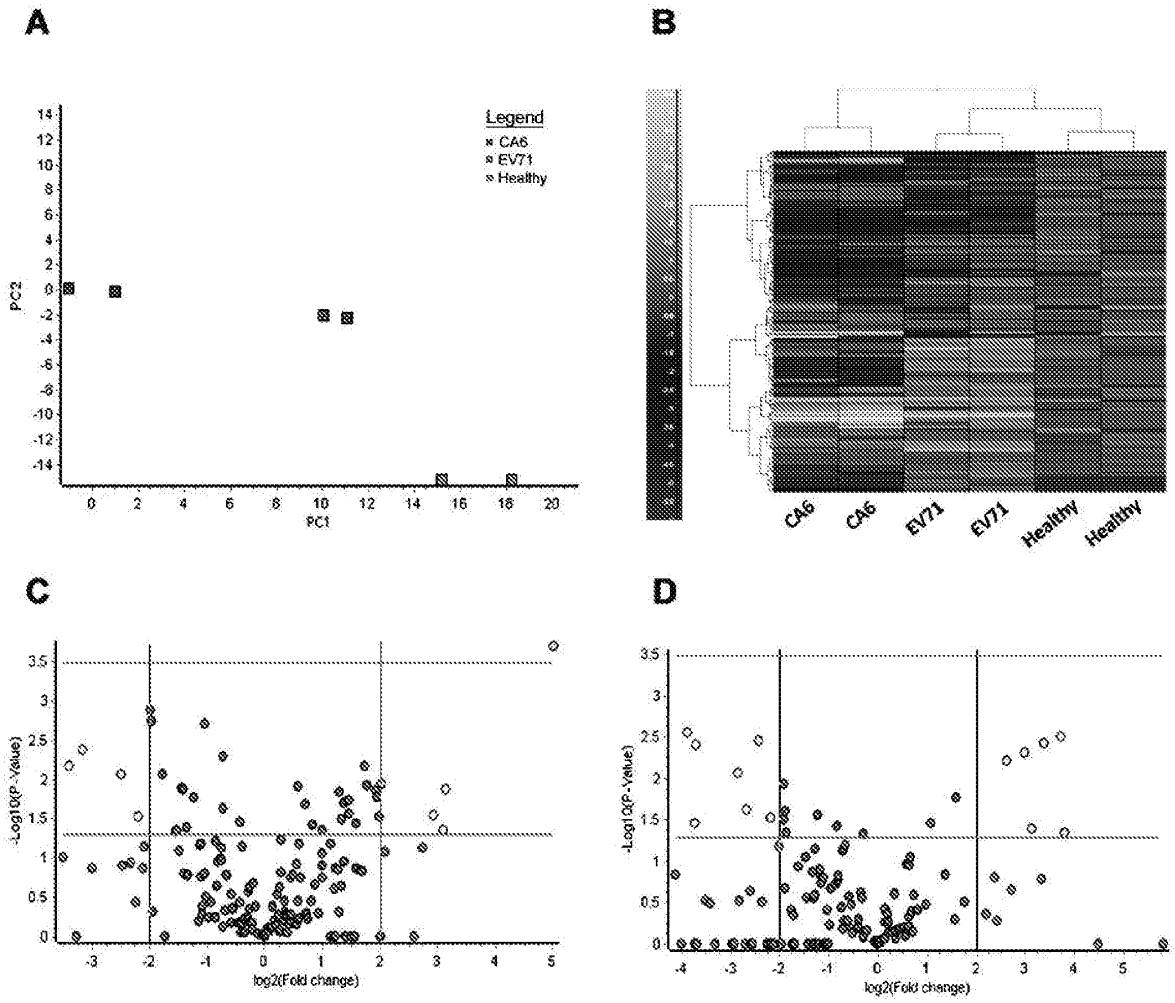

A
B
C
D
Legend
CA6
EV71
Healthy
PC1
PC2
CA6
CA6
EV71
EV71
Healthy
Healthy
-Log10(P-Value)
log2(Fold change)

Figure 12

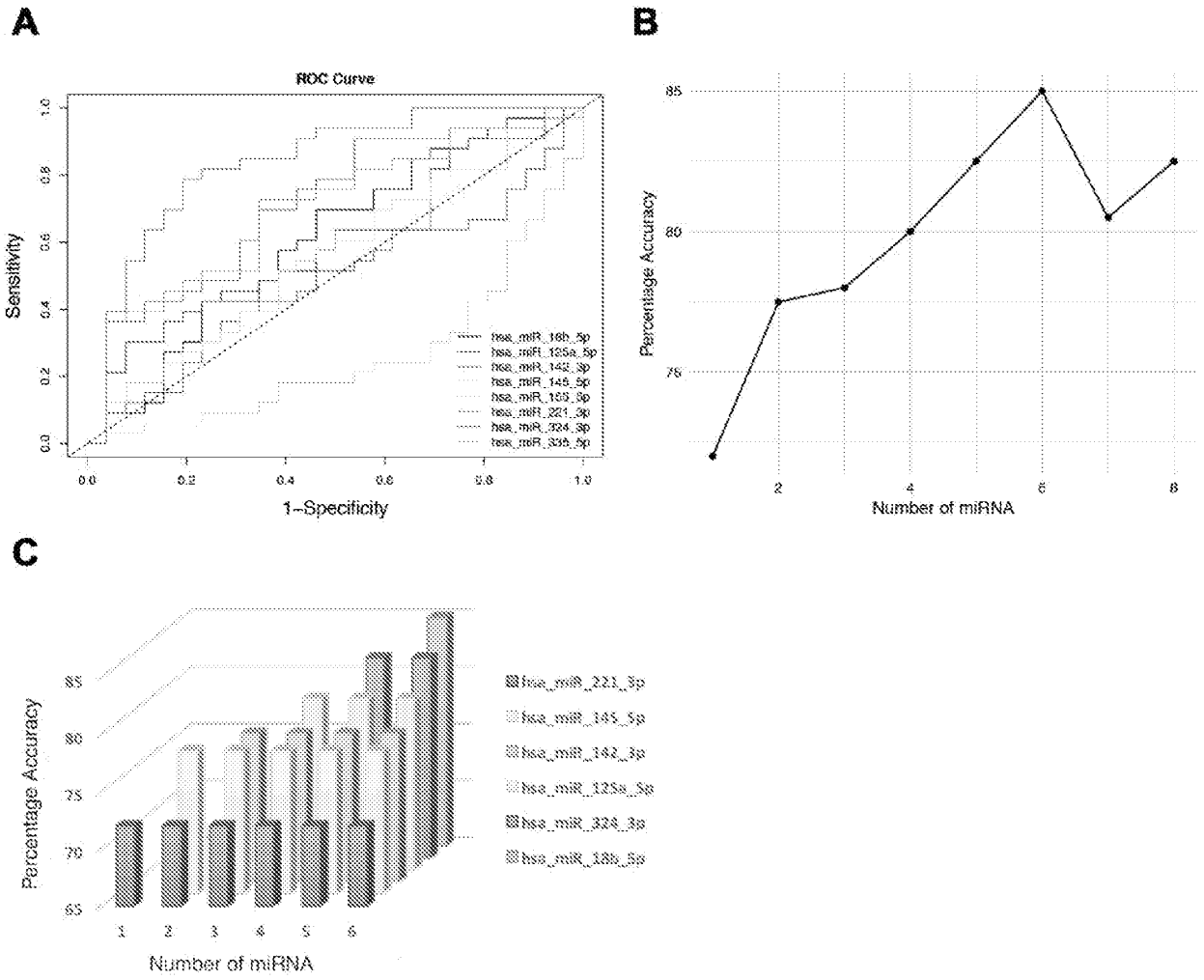

A
ROC Curve
Sensitivity
1−Specificity
hsa_miR_16b_5p
hsa_miR_125a_5p
hsa_miR_142_3p
hsa_miR_145_5p
hsa_miR_150_3p
hsa_miR_221_3p
hsa_miR_324_3p
hsa_miR_335_5p
B
Percentage Accuracy
Number of miRNA
C
Percentage Accuracy
Number of miRNA
hsa_miR_221_3p
hsa_miR_145_5p
hsa_miR_142_3p
hsa_miR_125a_5p
hsa_miR_324_3p
hsa_miR_16b_5p

Figure 13

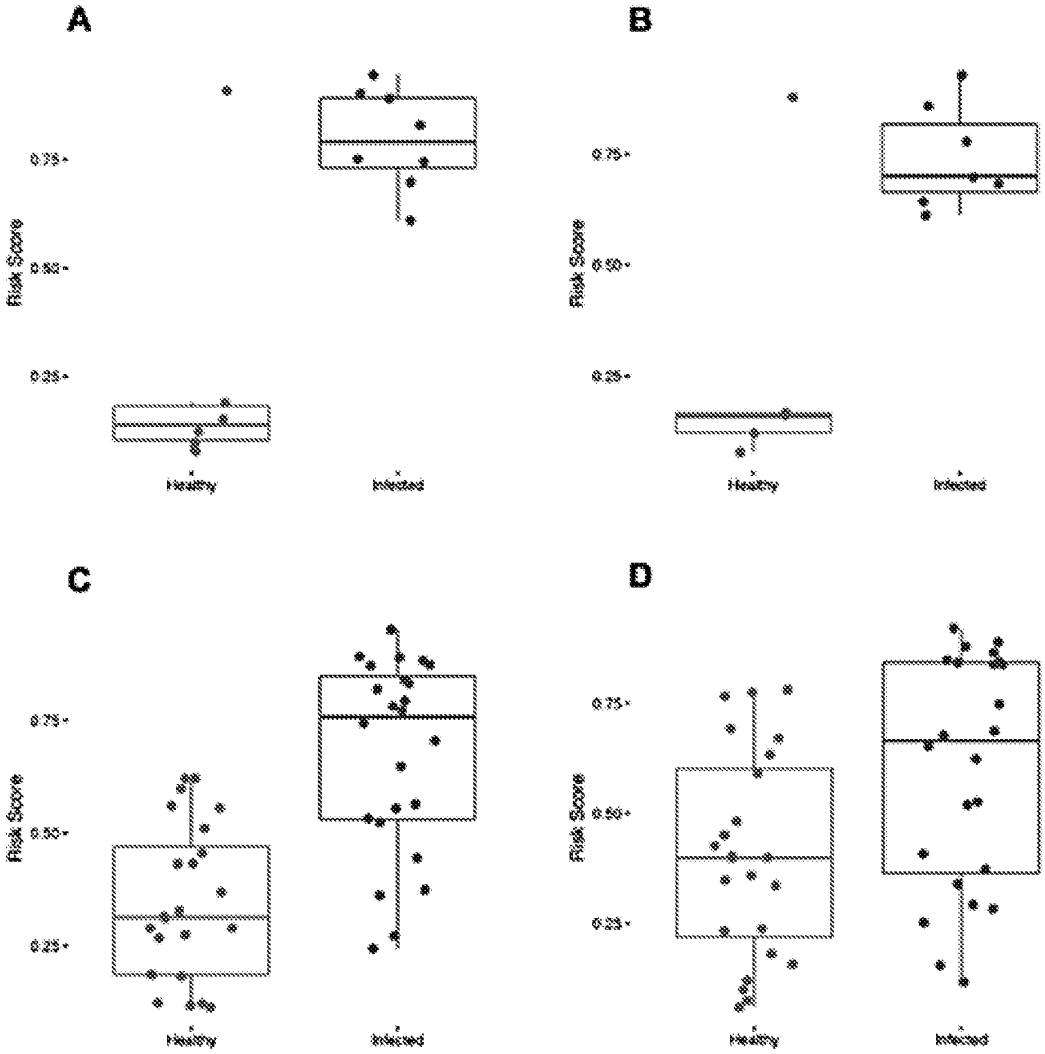


Figure 14

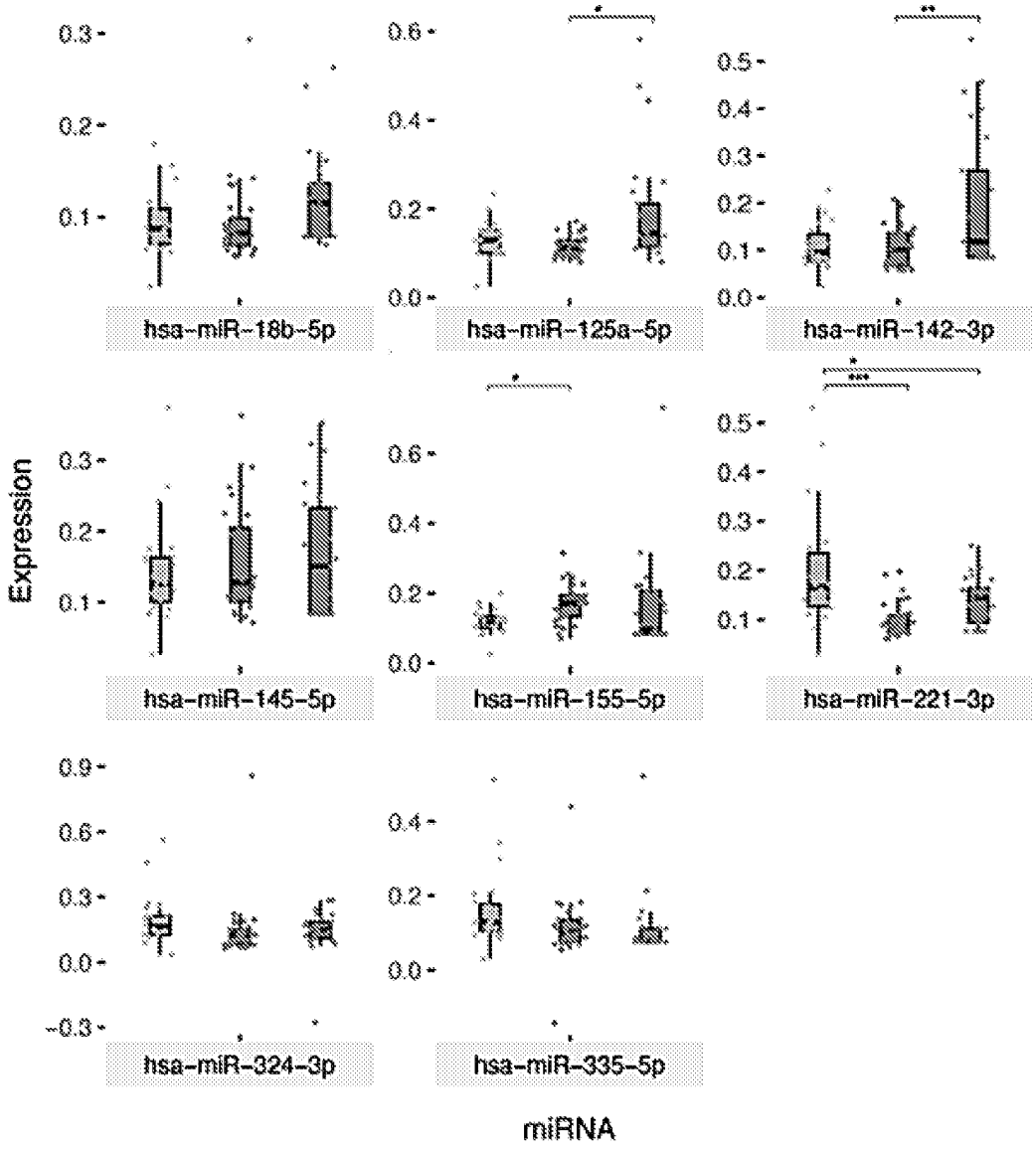

Expression
hsa-miR-18b-5p
hsa-miR-125a-5p
hsa-miR-142-3p
hsa-miR-145-5p
hsa-miR-155-5p
hsa-miR-221-3p
hsa-miR-324-3p
hsa-miR-335-5p
miRNA

Figure 15