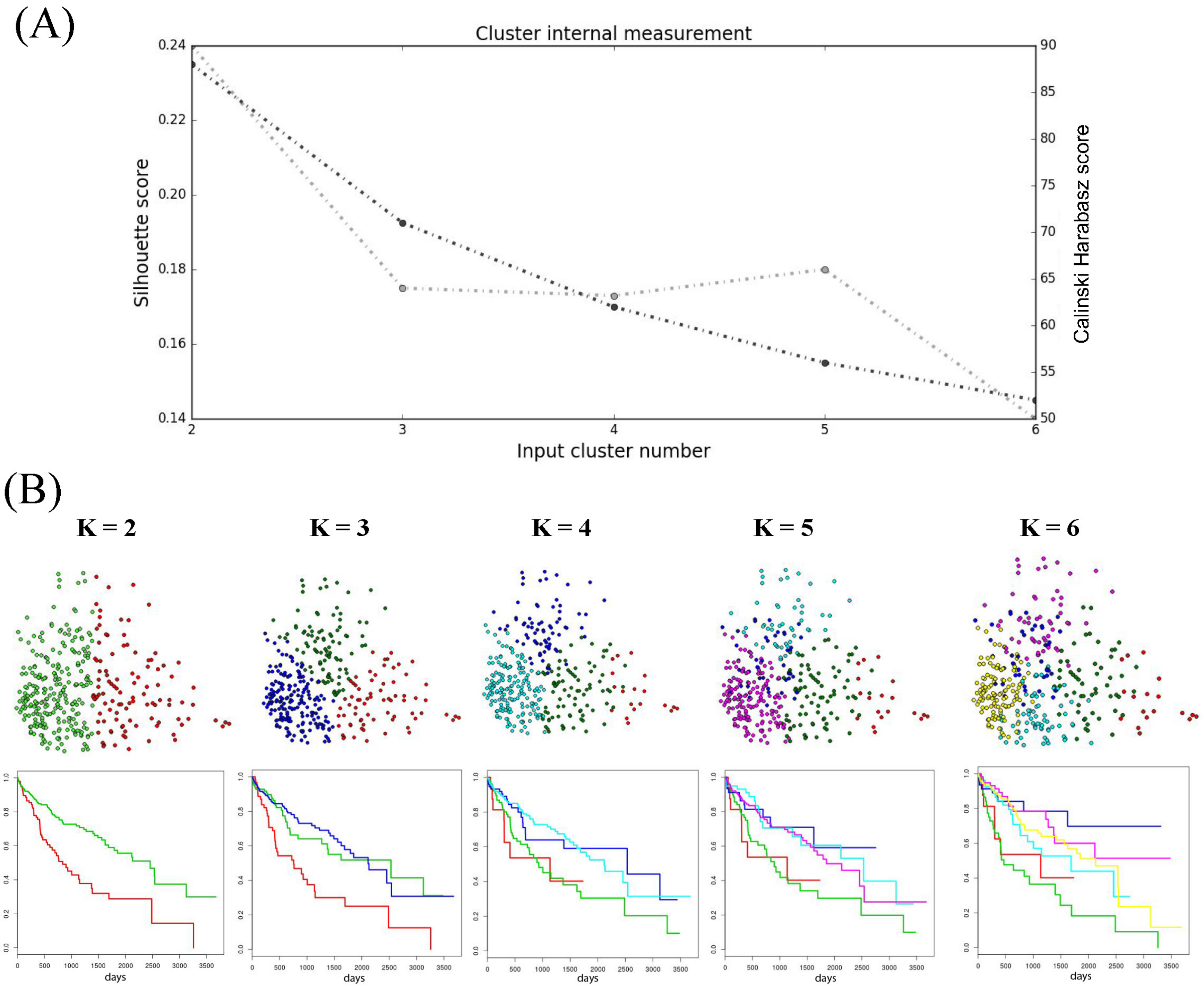
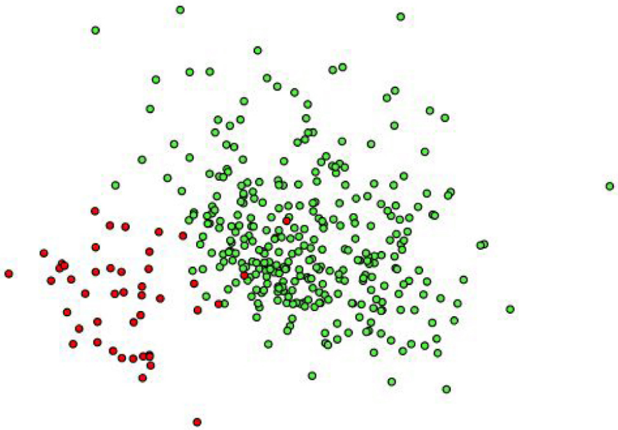

(A)
Cluster internal measurement
Silhouette score
0.24
0.22
0.20
0.18
0.16
0.14
Calinski Harabasz score
90
85
80
75
70
65
60
55
50
2
3
4
5
6
Input cluster number
(B)
K = 2
K = 3
K = 4
K = 5
K = 6
1.0
0.8
0.6
0.4
0.2
0.0
0
500
1000
1500
2000
2500
3000
3500
days

Supplementary Figure S1: (A) Selection of the best sub cluster K according to Silhouette score and Calinski-Harabasz score. (B) Kaplan-Meier plots show the separation of subtypes in terms of survival profiles from K=2 to 6.

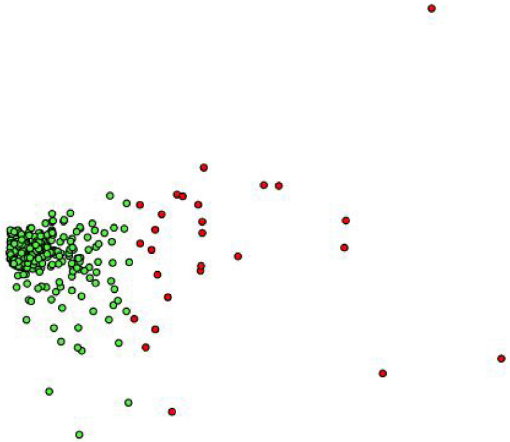


(A) PCA model using 100 components

Clusters	patients
Low survival	45
High survival	315

Components linked to survival:13

Train p-value: 0.14

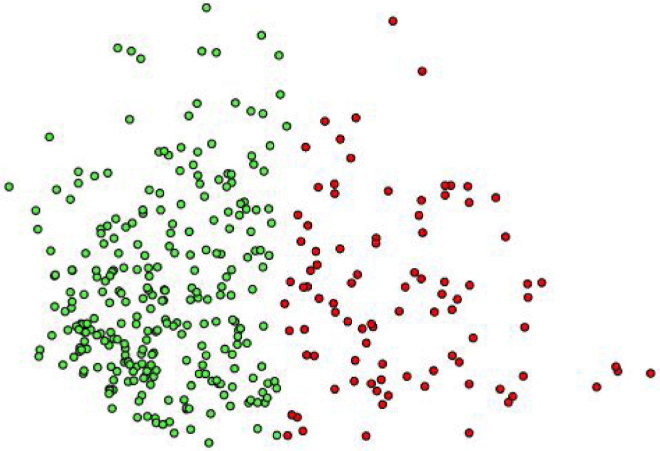


(B) CoxPH top 37 feature model

Clusters	patients
Low survival	38
High survival	322

Feature linked to survival:37

Train p-value: 3e-08



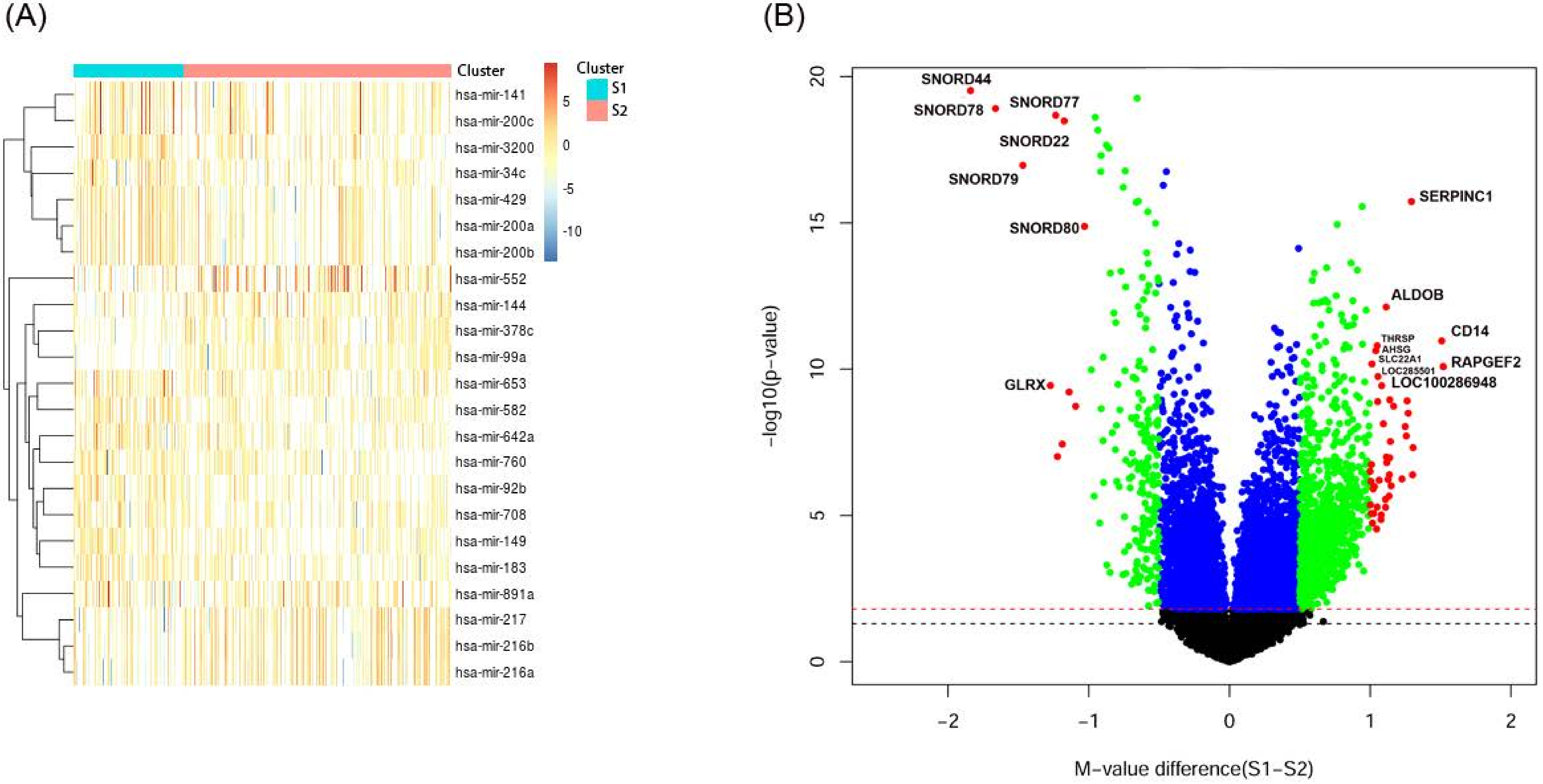
(C) Deep-Learning model

Clusters	patients
Low survival	105
High survival	255

Feature linked to survival: 37

Train p-value: 6e-09

Supplementary Figure S2: Comparisons of alternative methods with deep-learning based method in Figure 1. (A) Using top 100 principal components as supposed to 100 hidden nodes in deep learning, followed by subsequent Cox-PH and K-means clustering in Figure 1. (B) Using top 37 features from the 3 omics layers, based on single-variant Cox-PH models, followed by K-means clustering in Figure 1. (C) Deep learning based method in Figure 1.


(A)
Cluster
Cluster
S1
S2
5
0
-5
-10
hsa-mir-141
hsa-mir-200c
hsa-mir-3200
hsa-mir-34c
hsa-mir-429
hsa-mir-200a
hsa-mir-200b
hsa-mir-552
hsa-mir-144
hsa-mir-378c
hsa-mir-99a
hsa-mir-653
hsa-mir-582
hsa-mir-642a
hsa-mir-760
hsa-mir-92b
hsa-mir-708
hsa-mir-149
hsa-mir-183
hsa-mir-891a
hsa-mir-217
hsa-mir-216b
hsa-mir-216a
(B)
SNORD44
SNORD78
SNORD77
SNORD22
SNORD79
SNORD80
GLRX
SERPINC1
ALDOB
CD14
THRSP
AHSG
SLC22A1
LOC285501
RAPGEF2
LOC100286948
-log10(p-value)
20
15
10
5
0
-2
-1
0
1
2
M-value difference(S1-S2)

Supplementary Figure S3: Differential tests for miRNAs and Methylation (A) heatmap shows the differentially expressed miRNAs in two subtypes and (B) Volcano plot showing the differentially methylated genes in two subtypes. Red dotted line: BH adjusted p-value=0.05; blue dotted line: p-value=0.05 without adjustment. Red color: genes differentially methylated with BH adjusted p-value <0.05 and absolute mean difference >1 between the two subtypes.