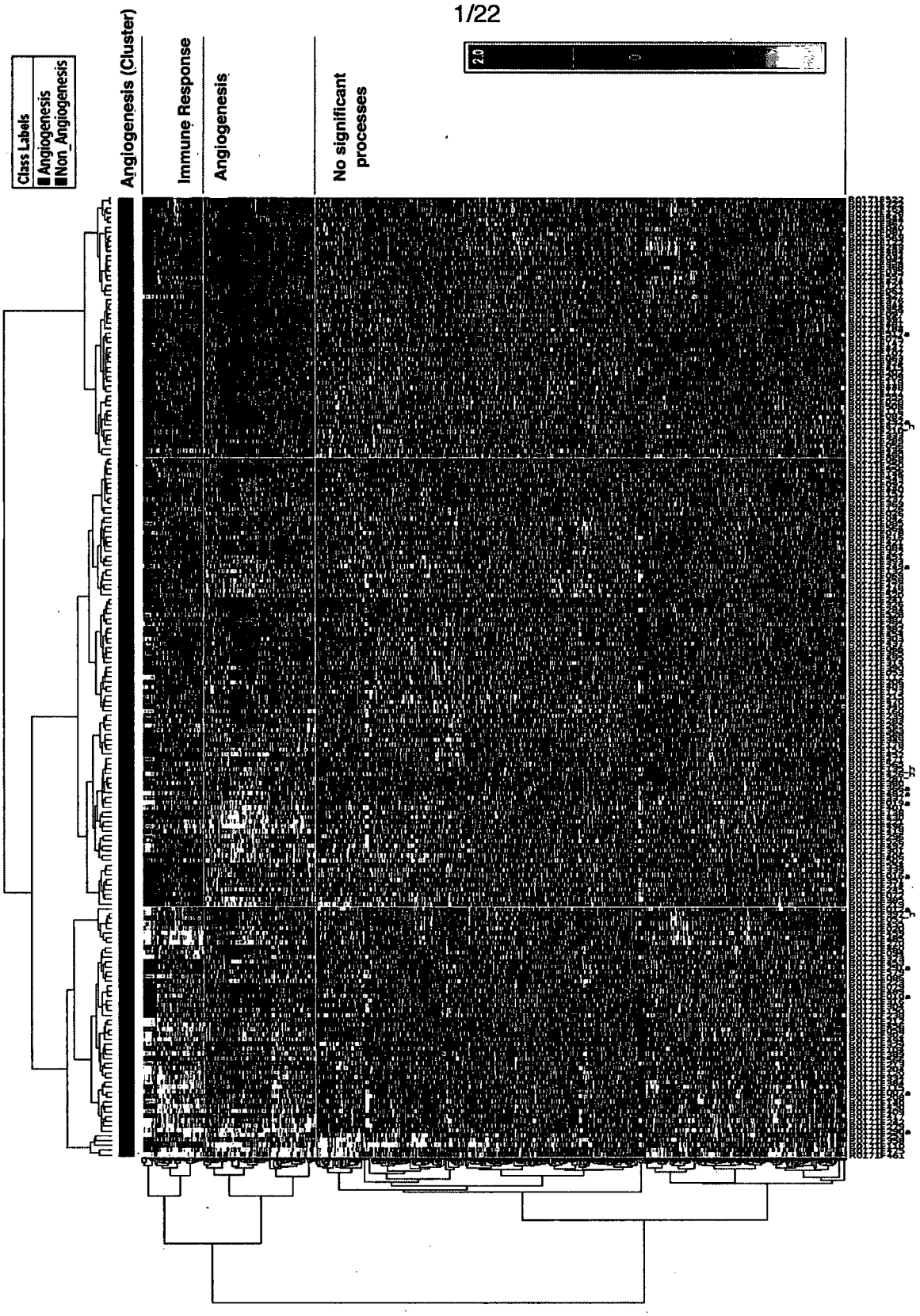

Class Labels
Angiogenesis
Non_Angiogenesis
Angiogenesis (Cluster)
Immune Response
Angiogenesis
No significant processes
2.0

Figure 1

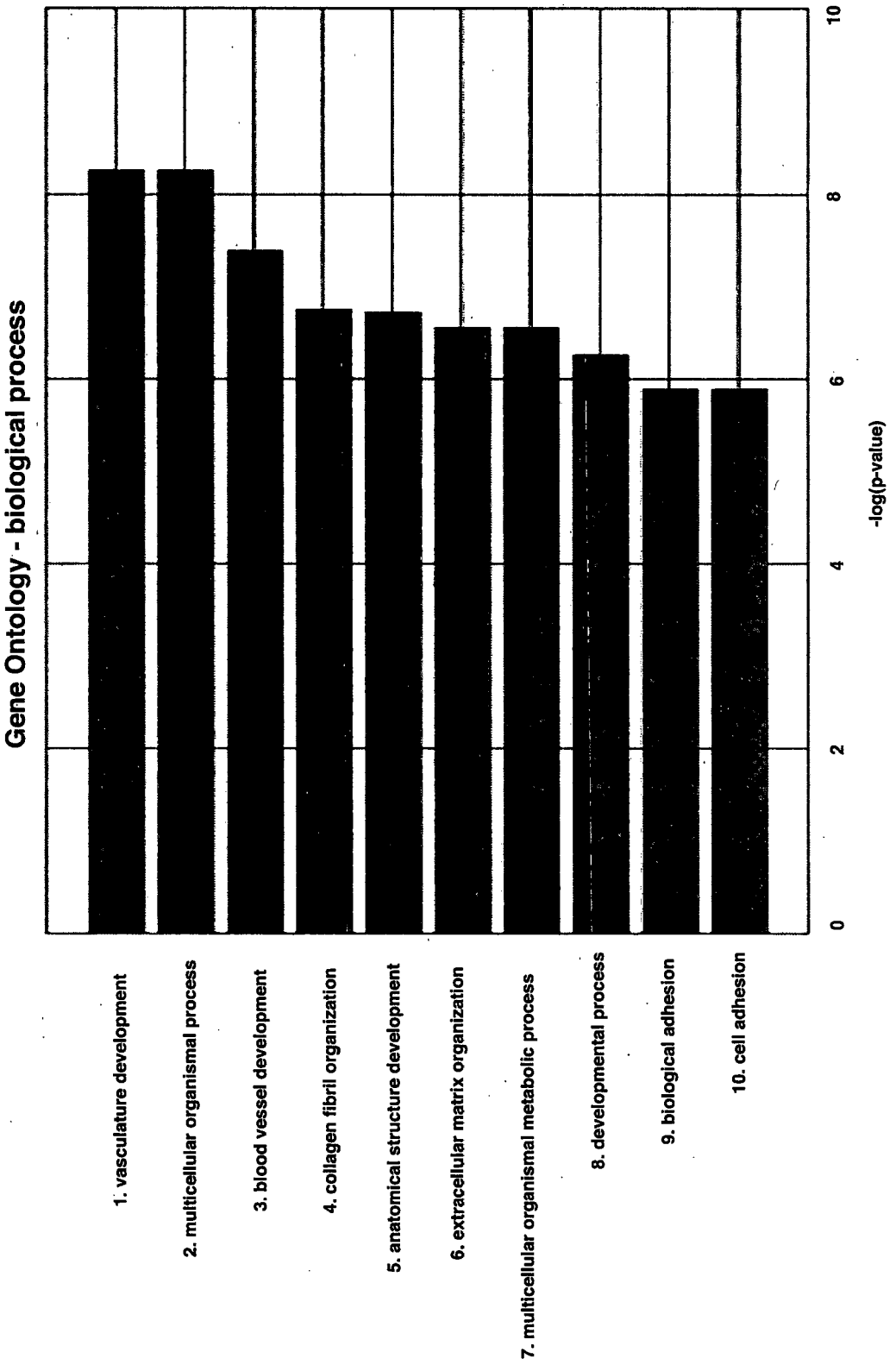

Gene Ontology - biological process
0
2
4
6
8
10
-log(p-value)
1. vasculature development
2. multicellular organismal process
3. blood vessel development
4. collagen fibril organization
5. anatomical structure development
6. extracellular matrix organization
7. multicellular organismal metabolic process
8. developmental process
9. biological adhesion
10. cell adhesion

Figure 2

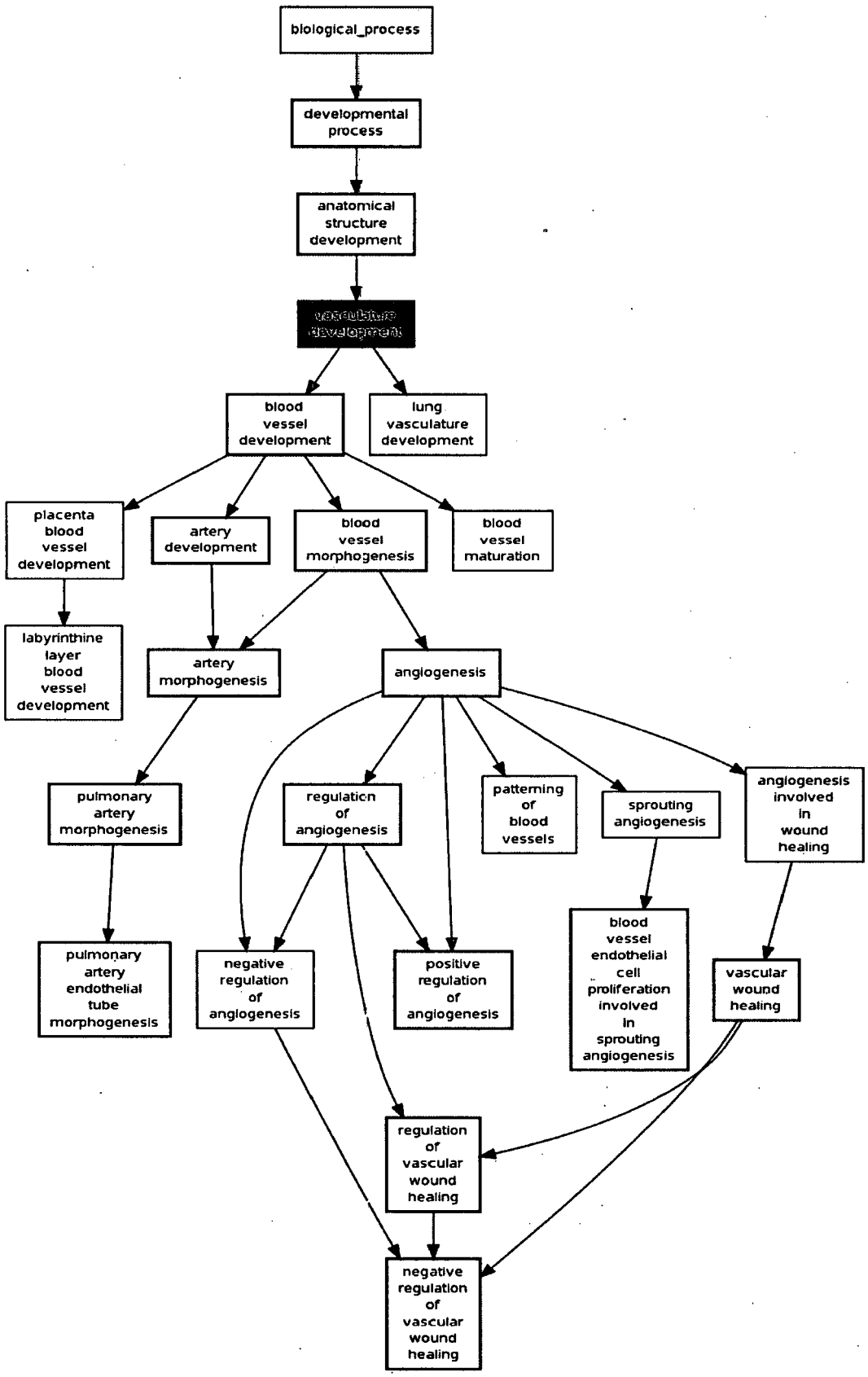

biological_process
developmental process
anatomical structure development
vasculature development
blood vessel development
lung vasculature development
placenta blood vessel development
artery development
blood vessel morphogenesis
blood vessel maturation
labyrinthine layer blood vessel development
artery morphogenesis
angiogenesis
pulmonary artery morphogenesis
regulation of angiogenesis
patterning of blood vessels
sprouting angiogenesis
angiogenesis involved in wound healing
pulmonary artery endothelial tube morphogenesis
negative regulation of angiogenesis
positive regulation of angiogenesis
blood vessel endothelial cell proliferation involved in sprouting angiogenesis
vascular wound healing
regulation of vascular wound healing
negative regulation of vascular wound healing

Figure 2B

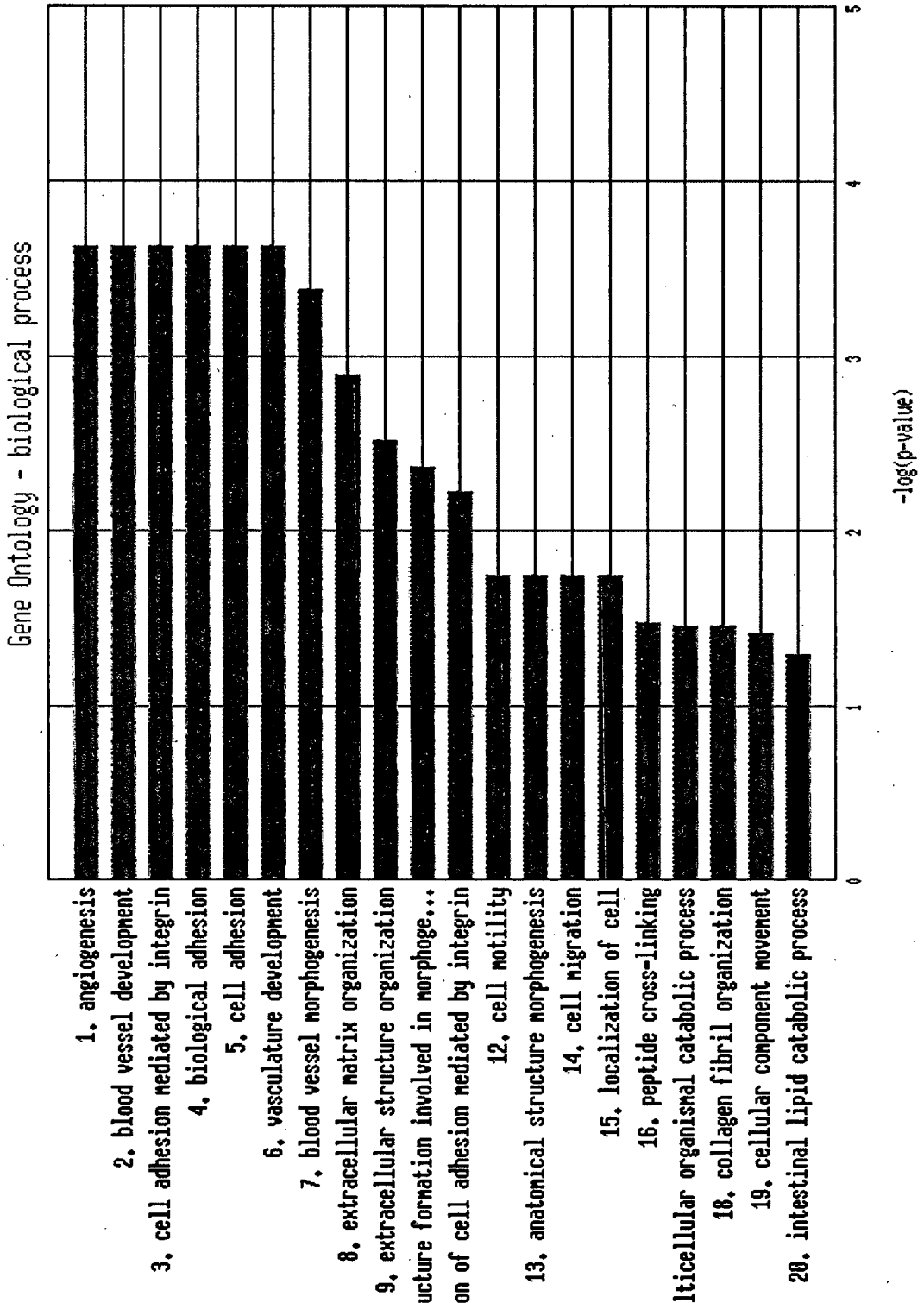

Gene Ontology - biological process
1. angiogenesis
2. blood vessel development
3. cell adhesion mediated by integrin
4. biological adhesion
5. cell adhesion
6. vasculature development
7. blood vessel morphogenesis
8. extracellular matrix organization
9. extracellular structure organization
10. anatomical structure formation involved in morphoge...
11. regulation of cell adhesion mediated by integrin
12. cell motility
13. anatomical structure morphogenesis
14. cell migration
15. localization of cell
16. peptide cross-linking
17. multicellular organismal catabolic process
18. collagen fibril organization
19. cellular component movement
20. intestinal lipid catabolic process
0
1
2
3
4
5
-log(p-value)

Figure 3

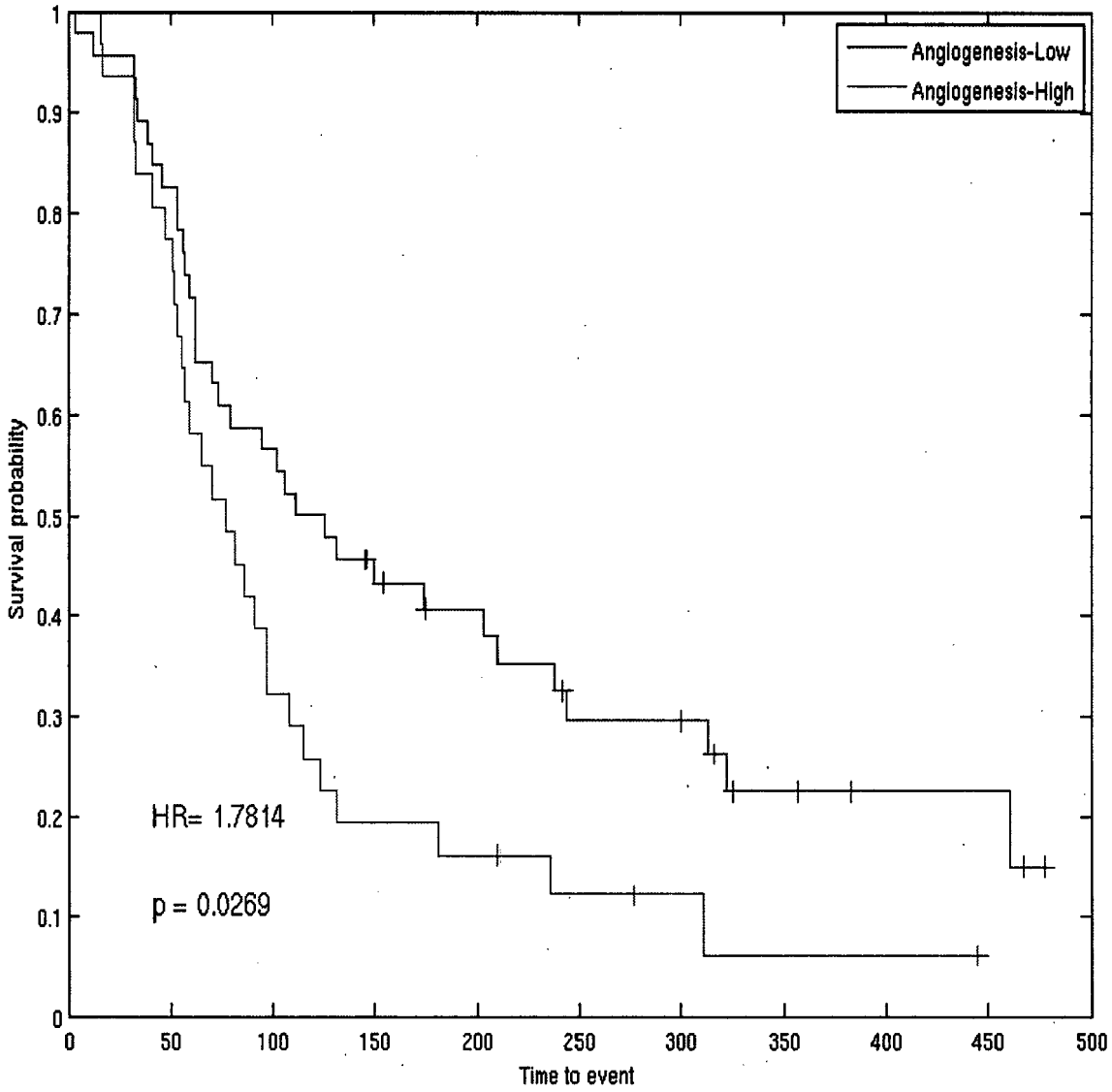

Angiogenesis-Low
Angiogenesis-High
Survival probability
Time to event
HR= 1.7814
p = 0.0269
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
0
50
100
150
200
250
300
350
400
450
500

Figure 4

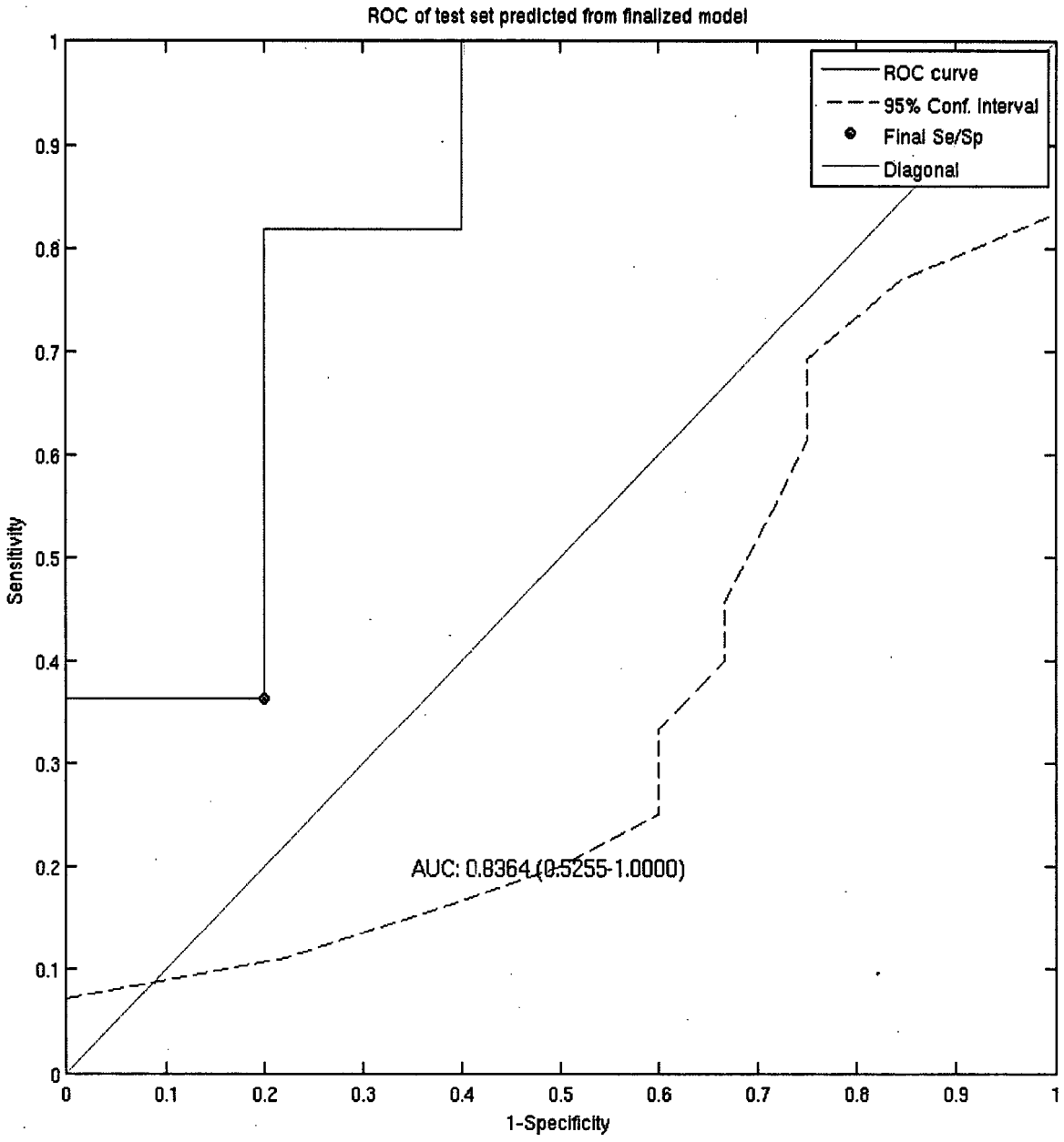

ROC of test set predicted from finalized model
ROC curve
95% Conf. Interval
Final Se/Sp
Diagonal
Sensitivity
1-Specificity
AUC: 0.8364 (0.5255-1.0000)
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1

Figure 5

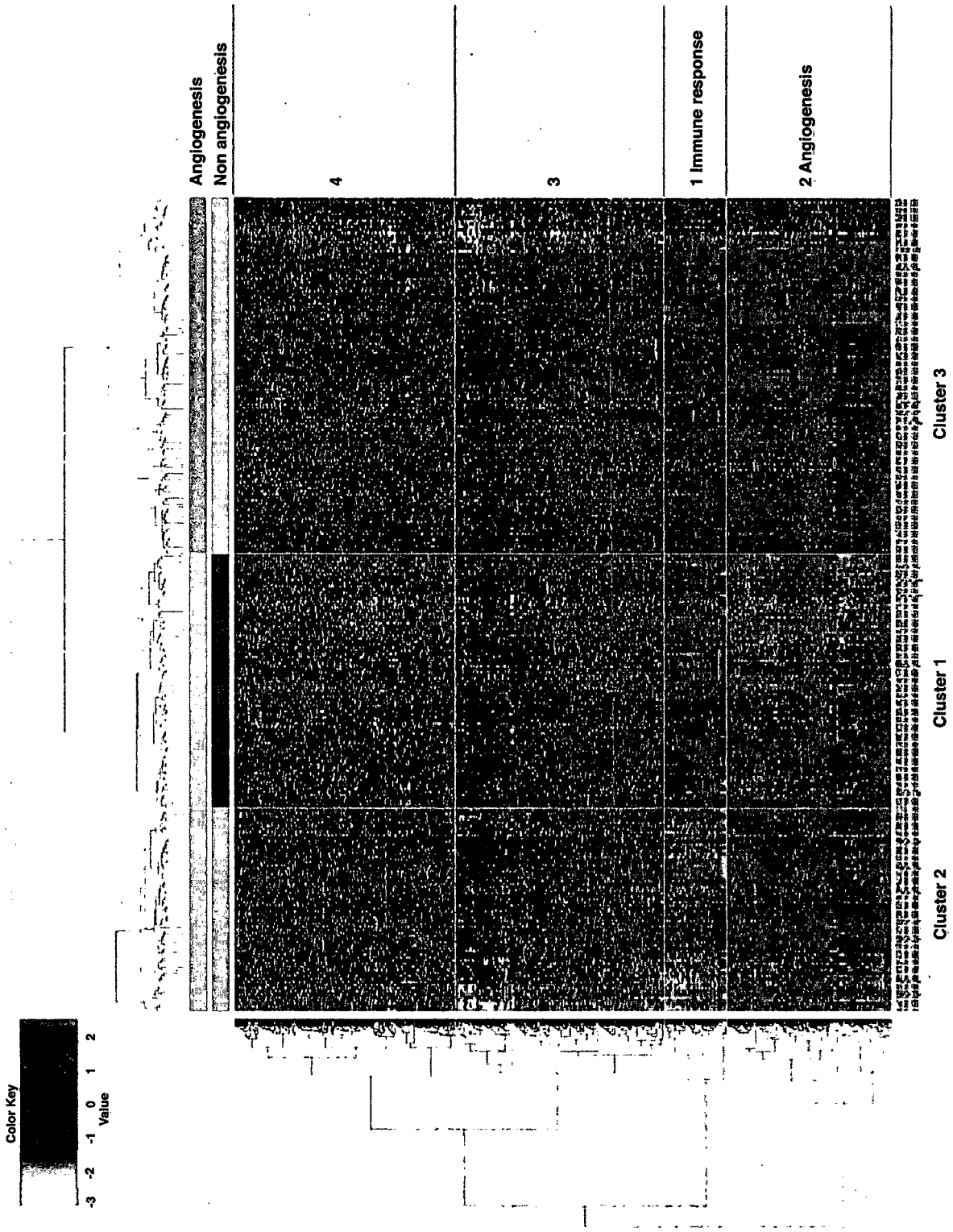

Angiogenesis
Non angiogenesis
4
3
1 Immune response
2 Angiogenesis
Cluster 3
Cluster 1
Cluster 2
Color Key
Value
-3
-2
-1
0
1
2

Figure 6

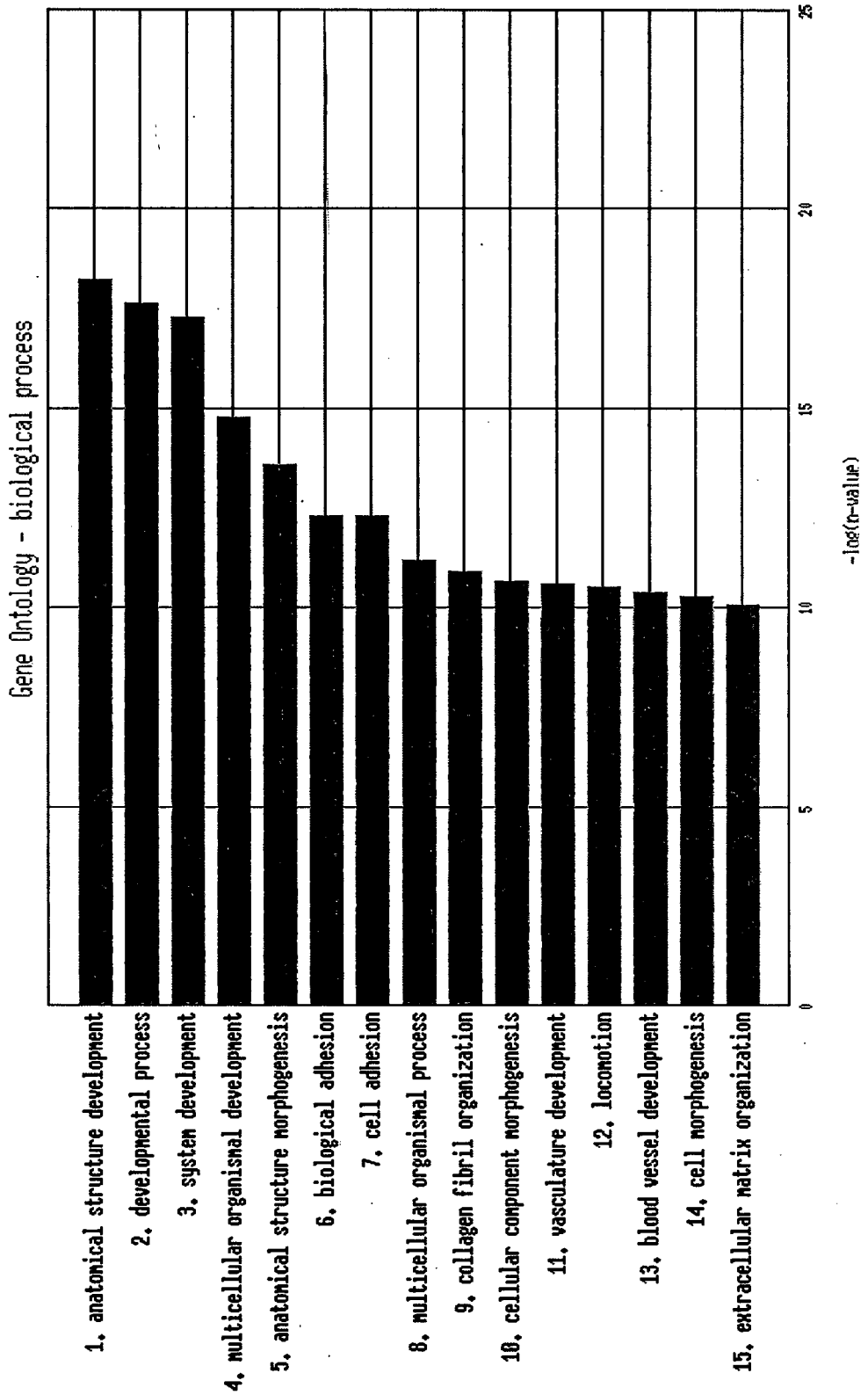

Gene Ontology - biological process
-log(p-value)
0
5
10
15
20
25
1. anatonical structure development
2. developmental process
3. system development
4. multicellular organismal development
5. anatomical structure morphogenesis
6. biological adhesion
7. cell adhesion
8. multicellular organismal process
9. collagen fibril organization
10. cellular component morphogenesis
11. vasculature development
12. locomotion
13. blood vessel development
14. cell morphogenesis
15. extracellular matrix organization

Figure 7A

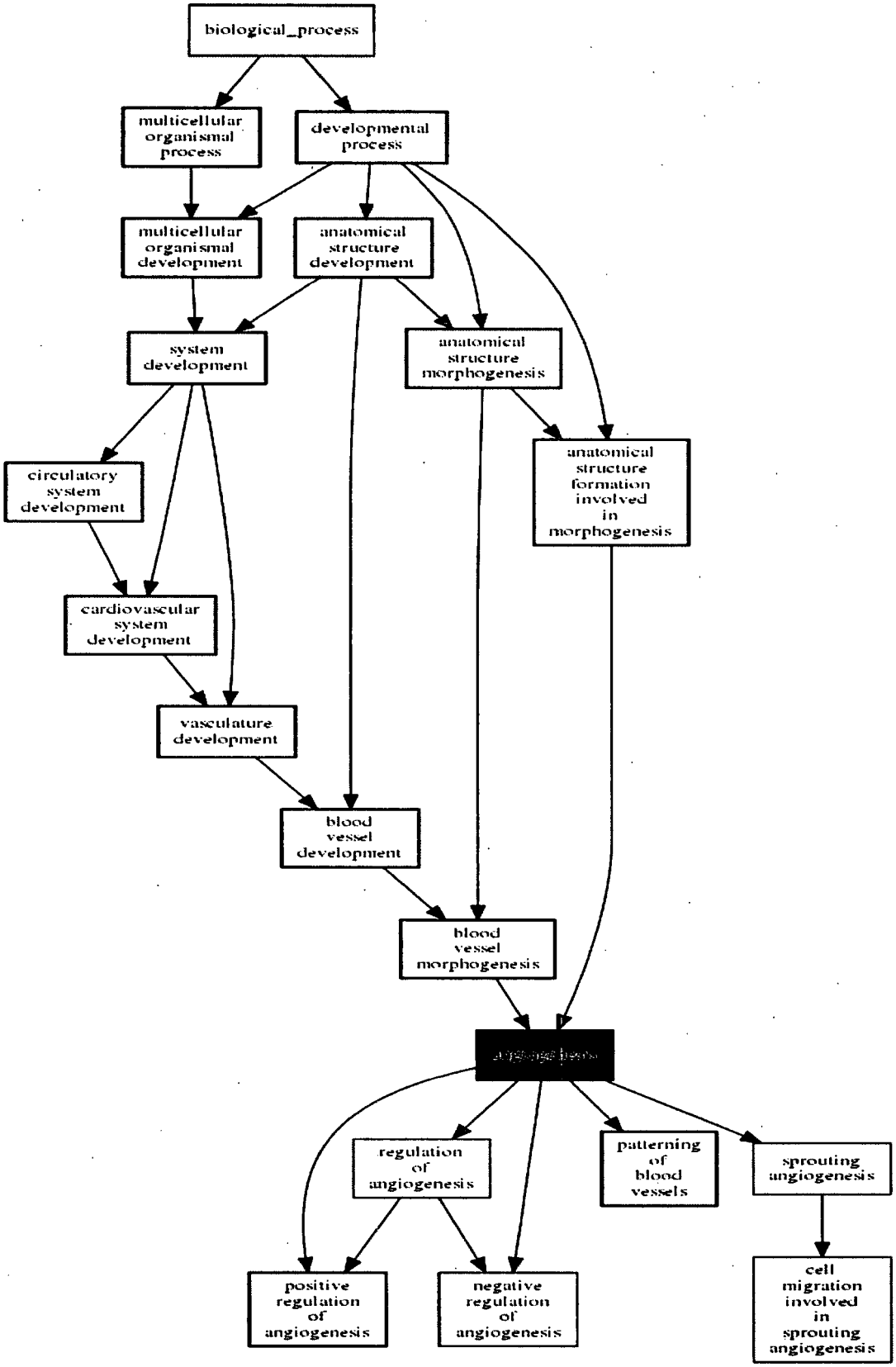

biological_process
multicellular organismal process
developmental process
multicellular organismal development
anatomical structure development
system development
anatomical structure morphogenesis
circulatory system development
anatomical structure formation involved in morphogenesis
cardiovascular system development
vasculature development
blood vessel development
blood vessel morphogenesis
regulation of angiogenesis
patterning of blood vessels
sprouting angiogenesis
positive regulation of angiogenesis
negative regulation of angiogenesis
cell migration involved in sprouting angiogenesis

Figure 7B

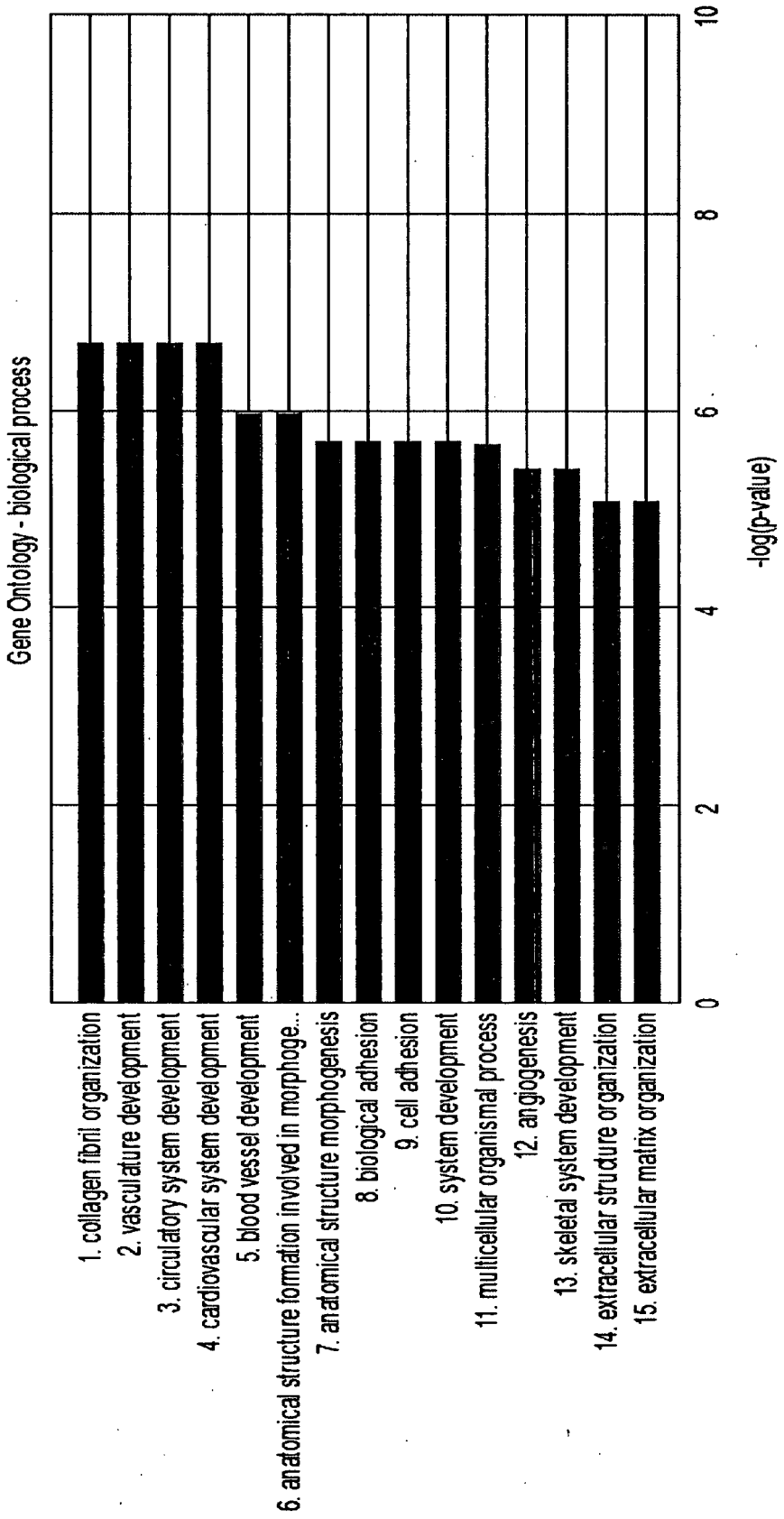

Gene Ontology - biological process
-log(p-value)
0
2
4
6
8
10
1. collagen fibril organization
2. vasculature development
3. circulatory system development
4. cardiovascular system development
5. blood vessel development
6. anatomical structure formation involved in morphoge...
7. anatomical structure morphogenesis
8. biological adhesion
9. cell adhesion
10. system development
11. multicellular organismal process
12. angiogenesis
13. skeletal system development
14. extracellular structure organization
15. extracellular matrix organization

Figure 8

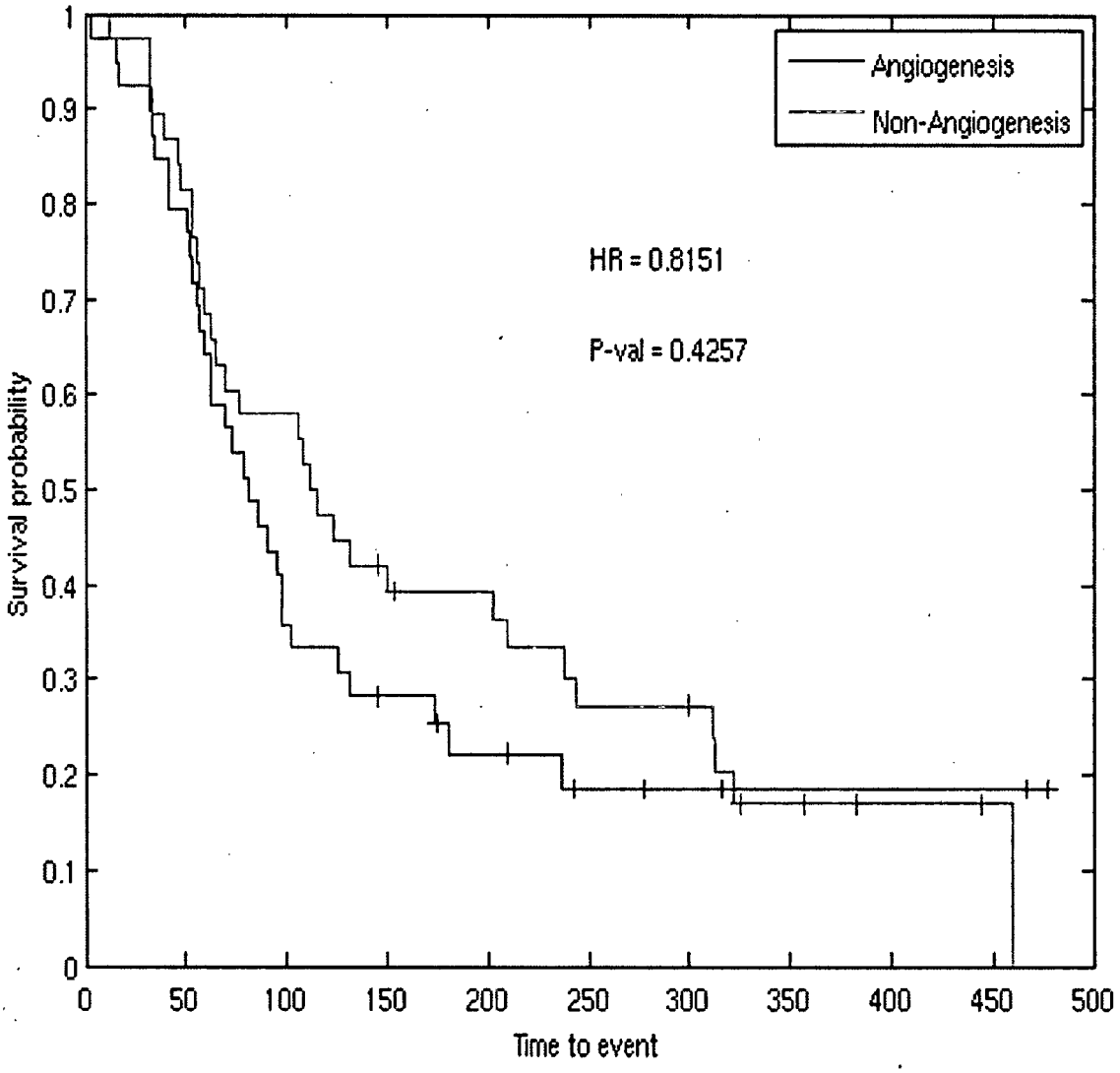

Angiogenesis
Non-Angiogenesis
HR = 0.8151
P-val = 0.4257
Survival probability
Time to event
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
0
50
100
150
200
250
300
350
400
450
500

Figure 9

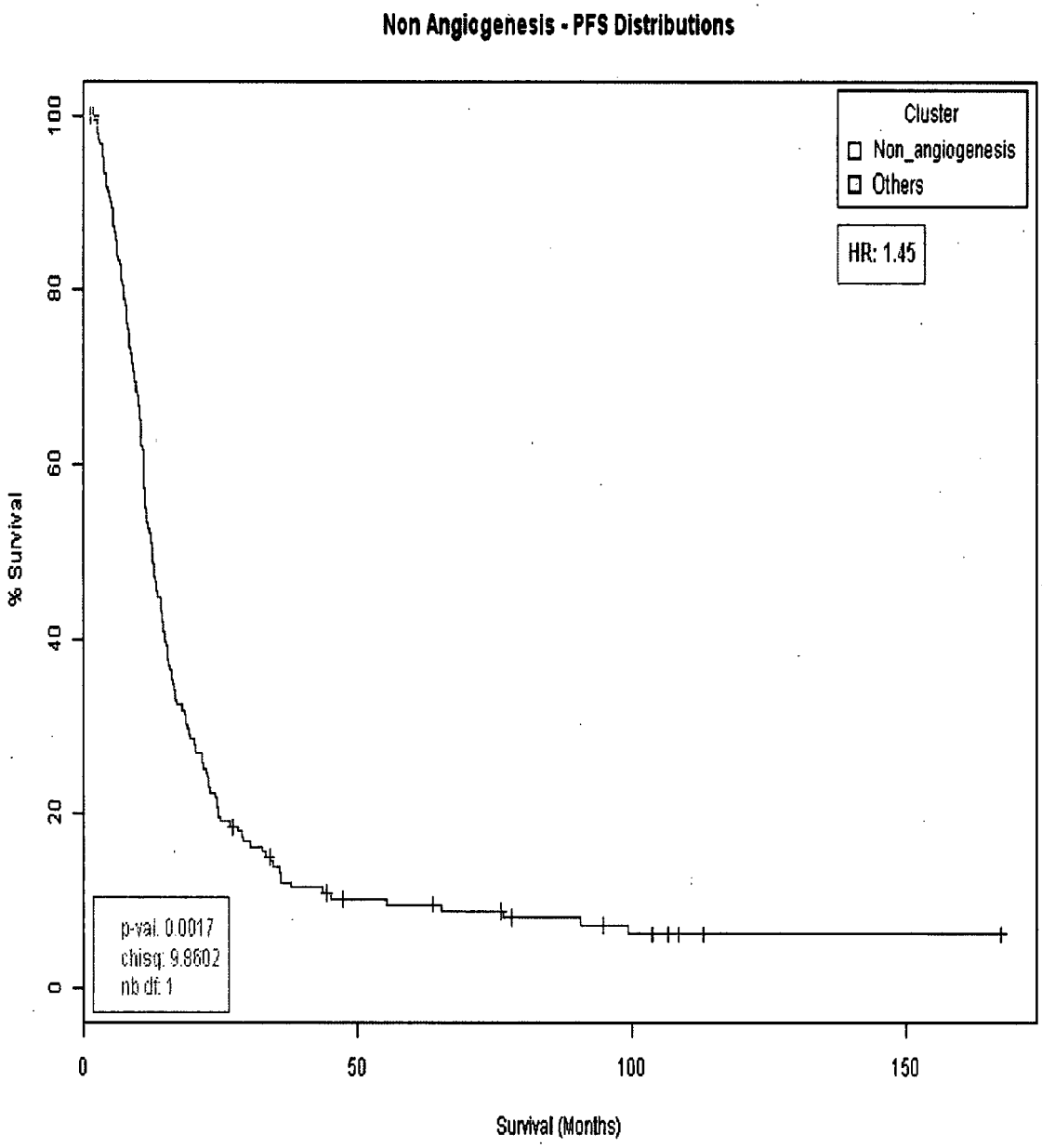

Non Angiogenesis - PFS Distributions
Cluster
Non_angiogenesis
Others
HR: 1.45
p-val: 0.0017
chisq: 9.8602
nb df: 1
% Survival
0
20
40
60
80
100
0
50
100
150
Survival (Months)

Figure 10

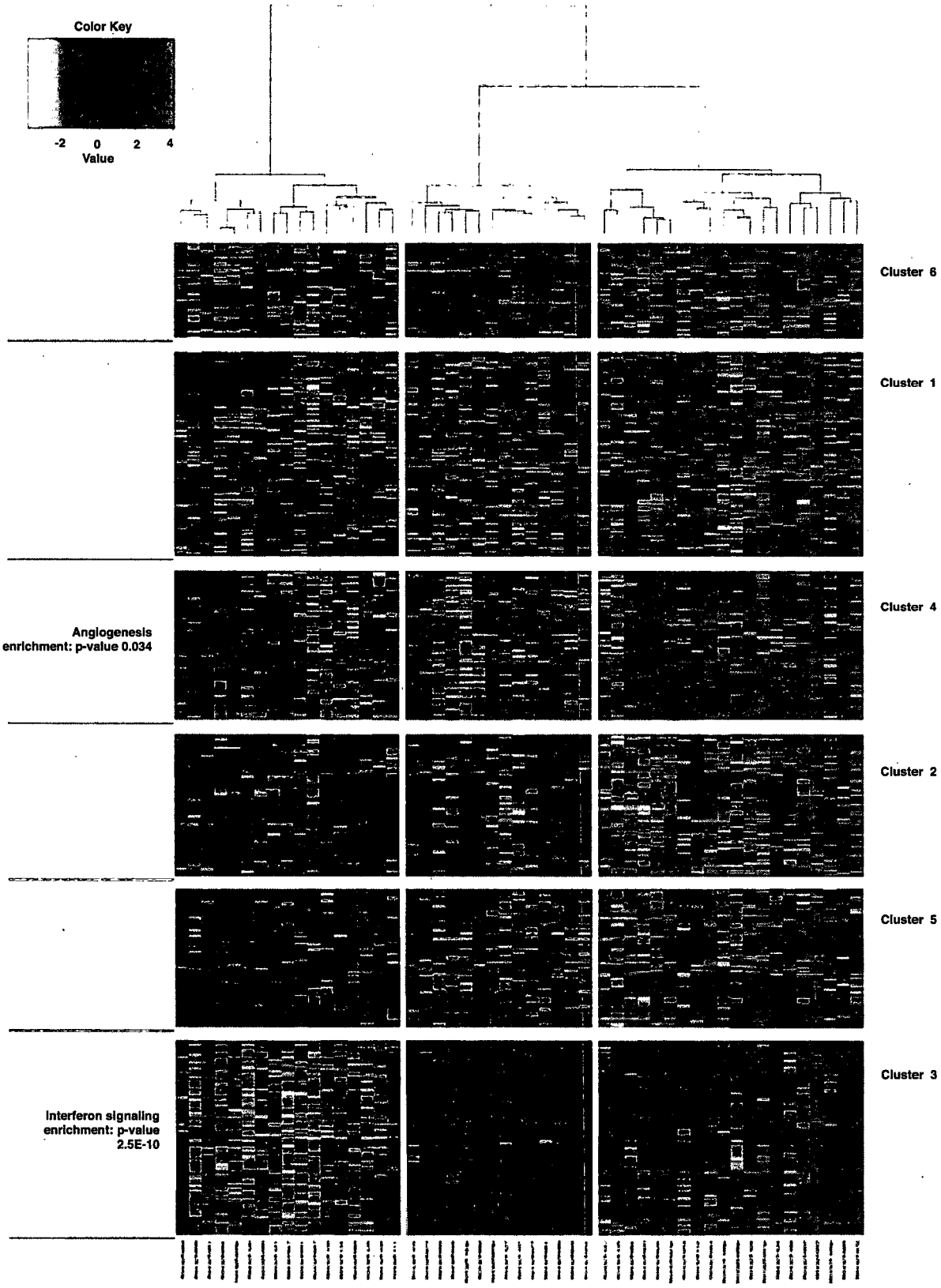

Color Key
-2 0 2 4
Value
Cluster 6
Cluster 1
Angiogenesis enrichment: p-value 0.034
Cluster 4
Cluster 2
Cluster 5
Interferon signaling enrichment: p-value 2.5E-10
Cluster 3

Figure 11A

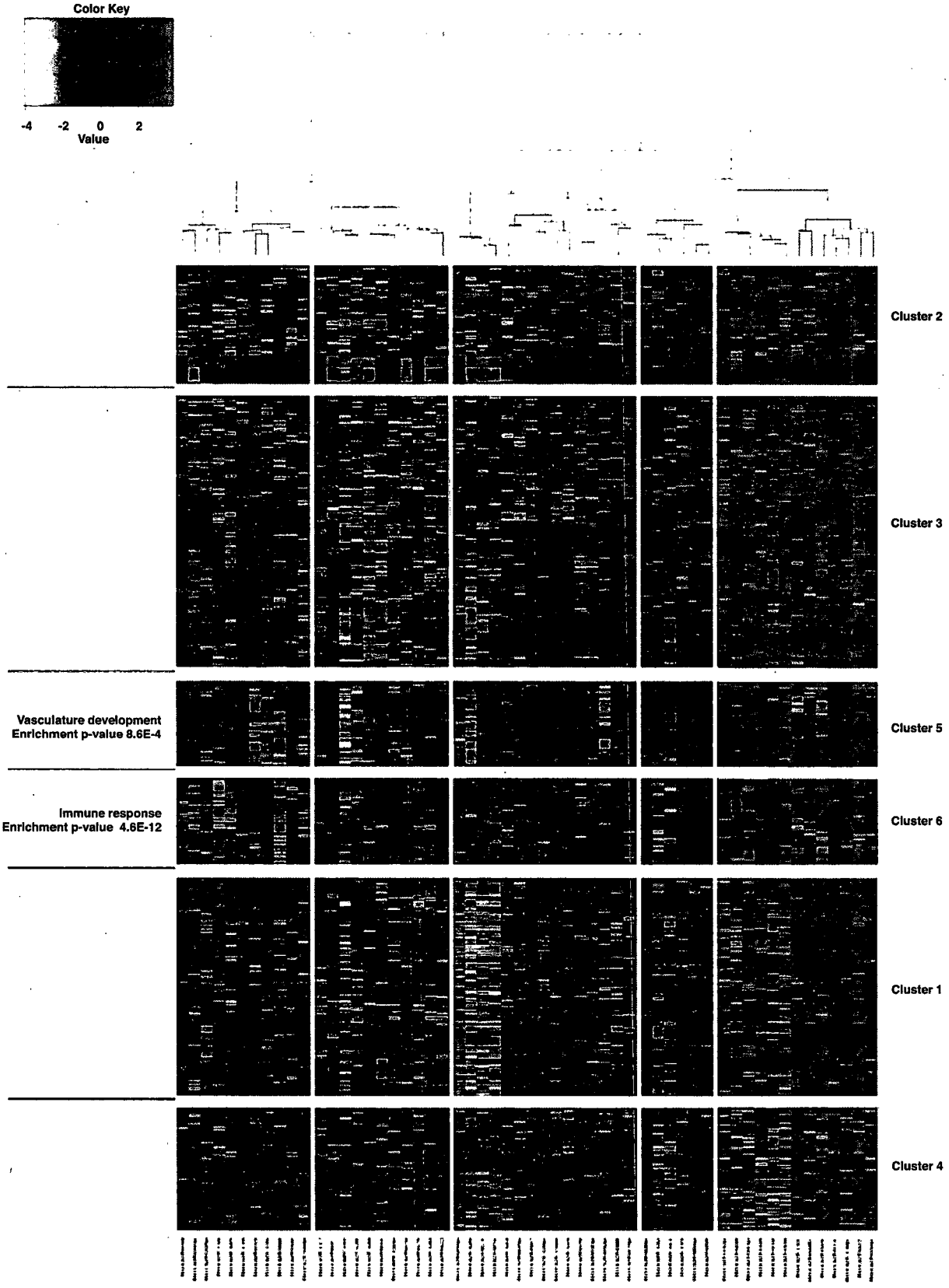

Color Key
-4
-2
0
2
Value
Cluster 2
Cluster 3
Vasculature development
Enrichment p-value 8.6E-4
Cluster 5
Immune response
Enrichment p-value 4.6E-12
Cluster 6
Cluster 1
Cluster 4

Figure 11B

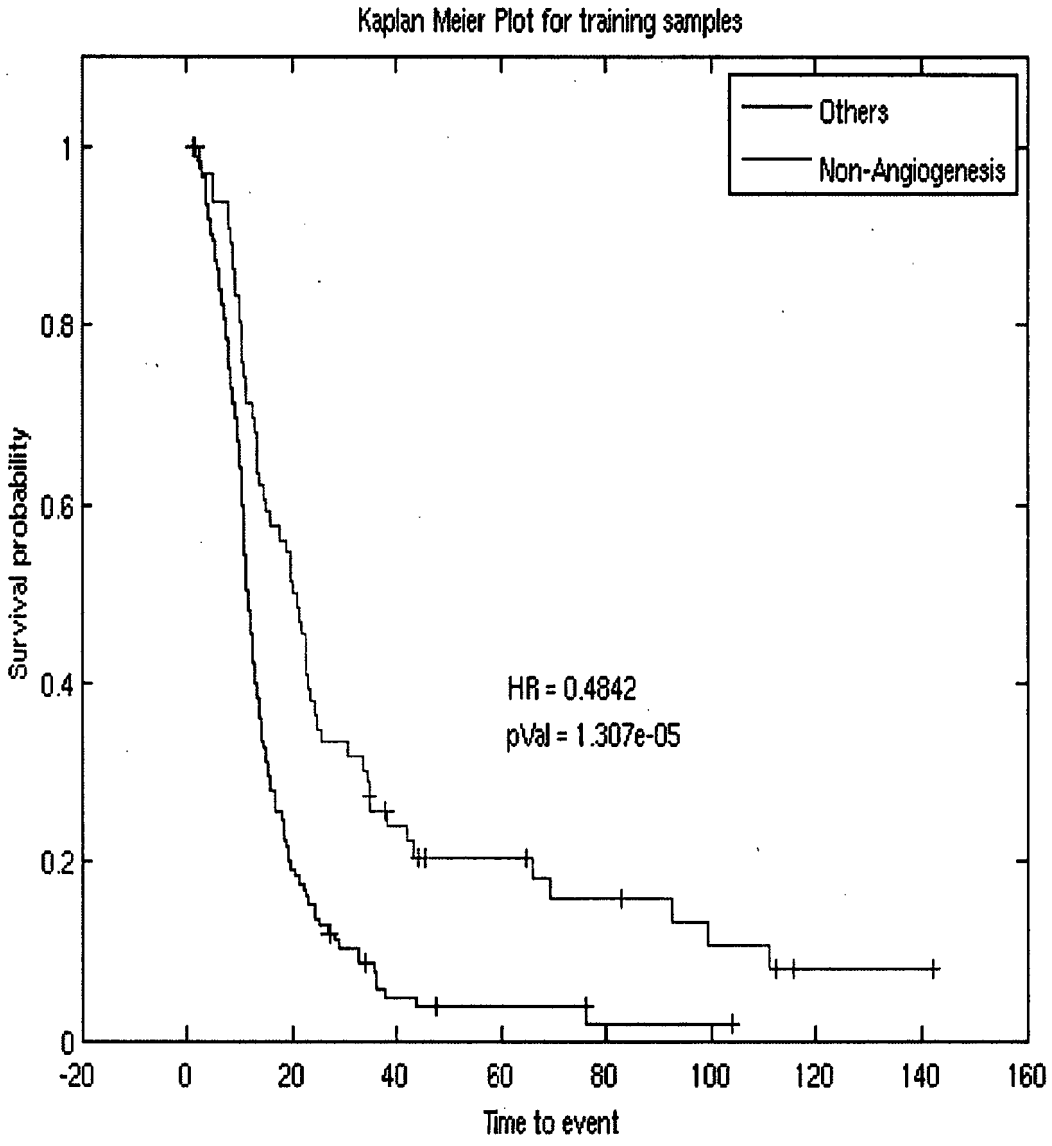

Kaplan Meier Plot for training samples
Others
Non-Angiogenesis
HR = 0.4842
pVal = 1.307e-05
Survival probability
Time to event
0
0.2
0.4
0.6
0.8
1
-20
0
20
40
60
80
100
120
140
160

Figure 12

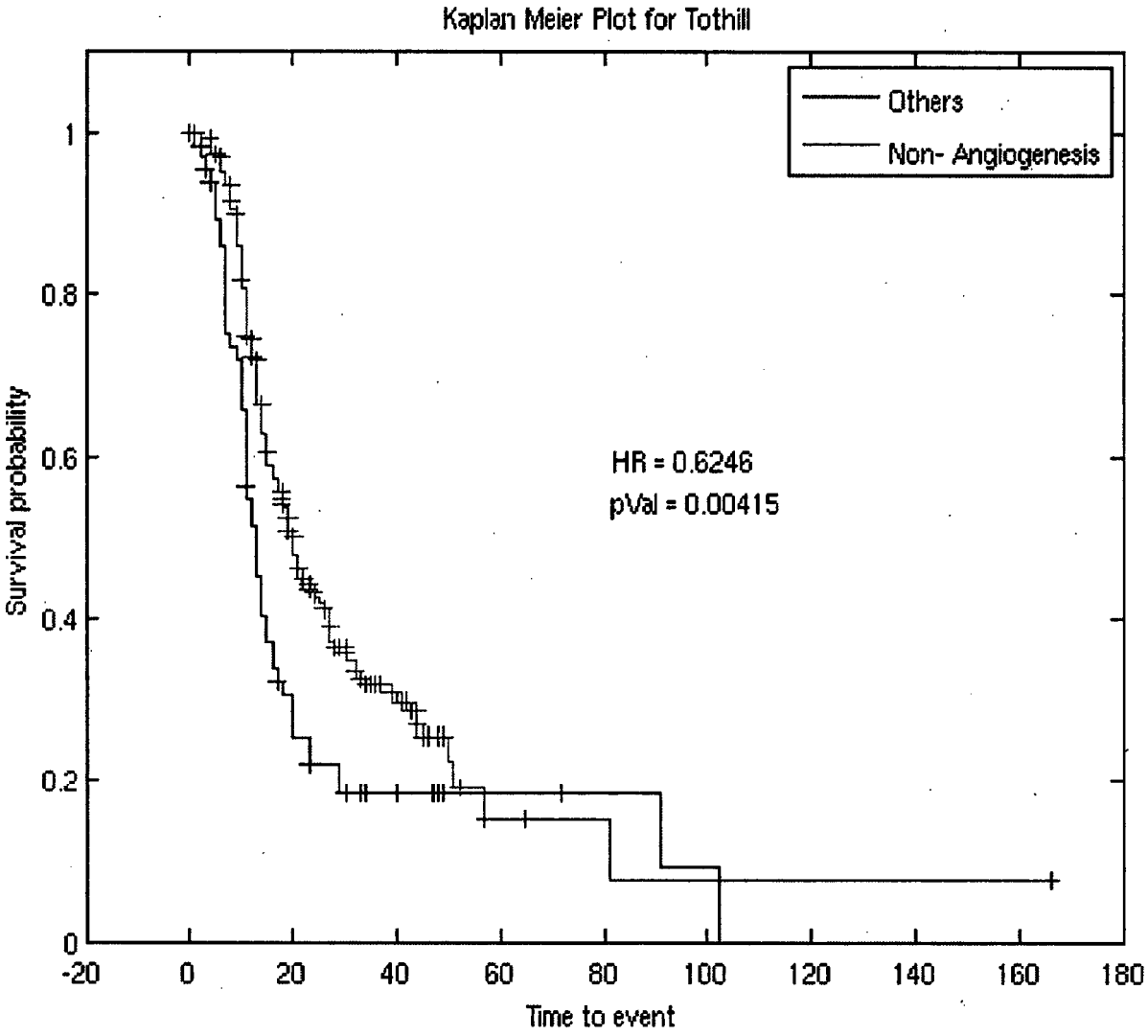
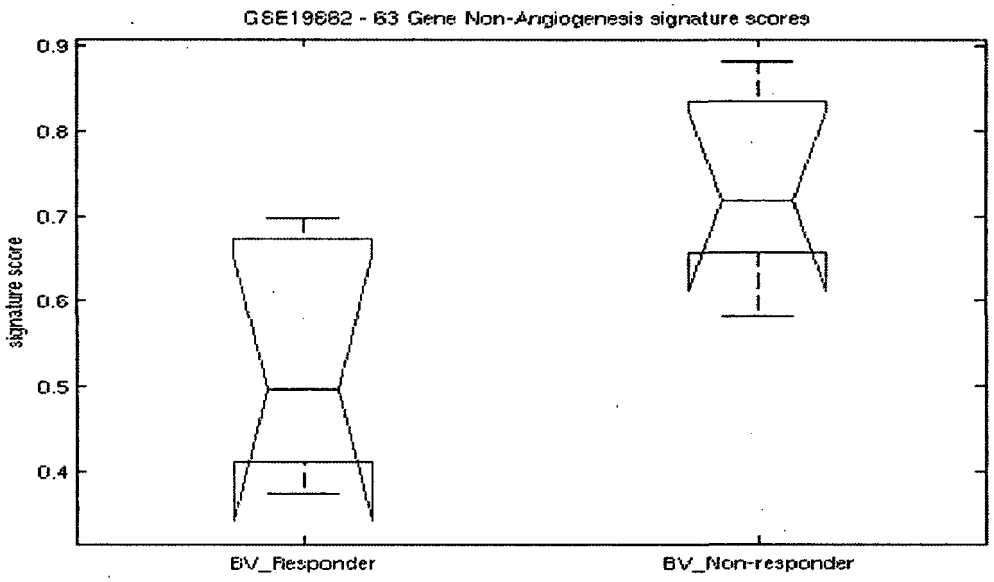

Kaplan Meier Plot for Tothill
Others
Non- Angiogenesis
HR = 0.6246
pVal = 0.00415
Survival probability
Time to event
0
0.2
0.4
0.6
0.8
1
-20
0
20
40
60
80
100
120
140
160
180

Figure 13

A.


GSE19862 - 63 Gene Non-Angiogenesis signature scores
signature score
0.9
0.8
0.7
0.6
0.5
0.4
BV_Responder
BV_Non-responder

B.

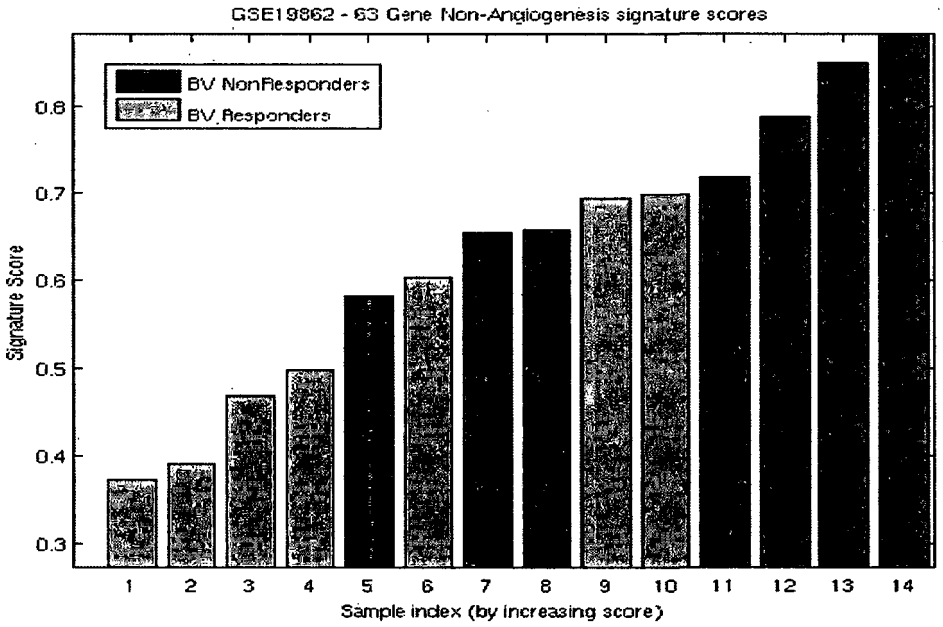

GSE19862 - 63 Gene Non-Angiogenesis signature scores
BV NonResponders
BV Responders
Signature Score
0.8
0.7
0.6
0.5
0.4
0.3
1 2 3 4 5 6 7 8 9 10 11 12 13 14
Sample index (by increasing score)

Figure 14

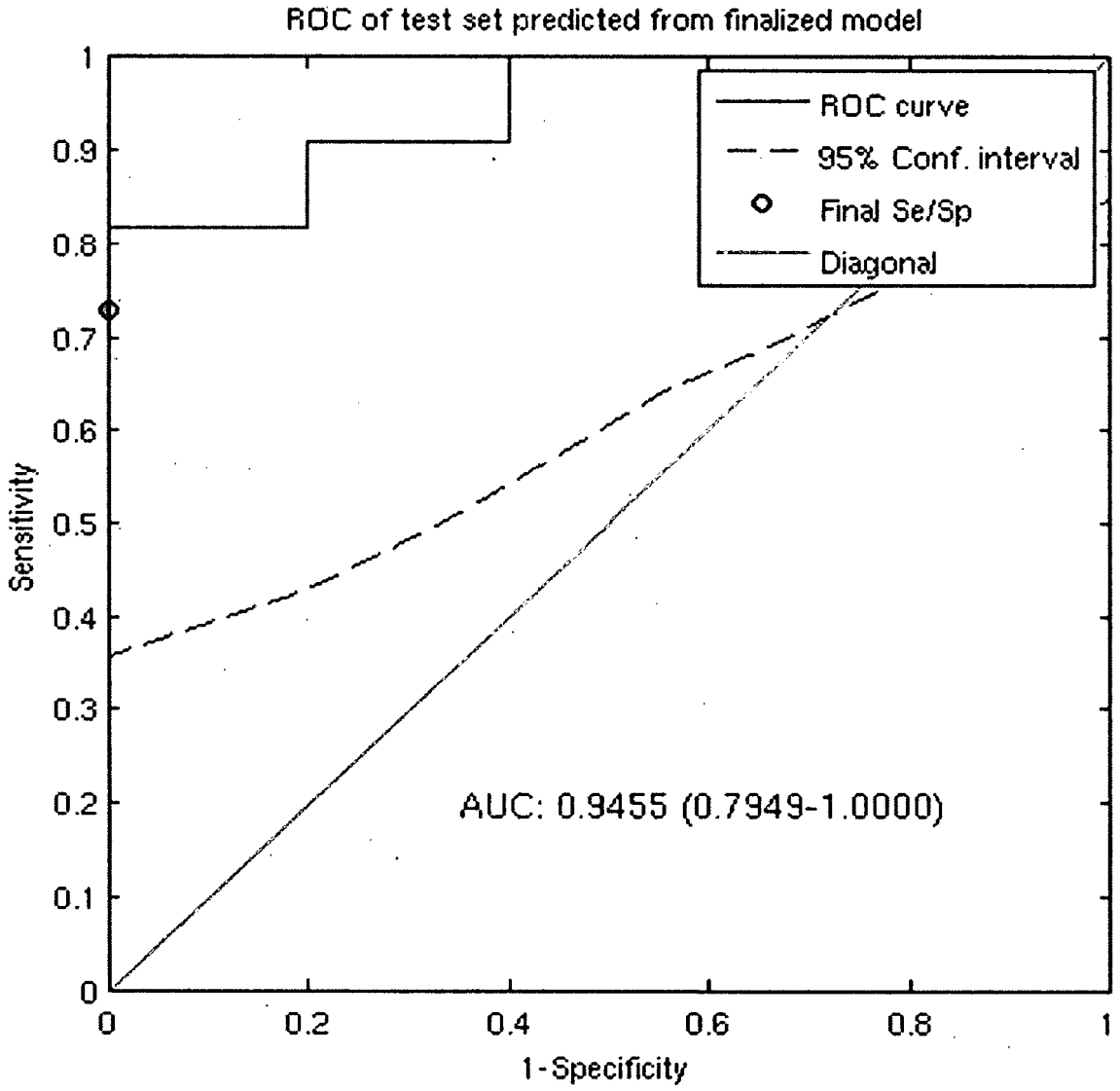

ROC of test set predicted from finalized model
ROC curve
95% Conf. interval
Final Se/Sp
Diagonal
AUC: 0.9455 (0.7949-1.0000)
Sensitivity
1-Specificity
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
0
0.2
0.4
0.6
0.8
1

Figure 15

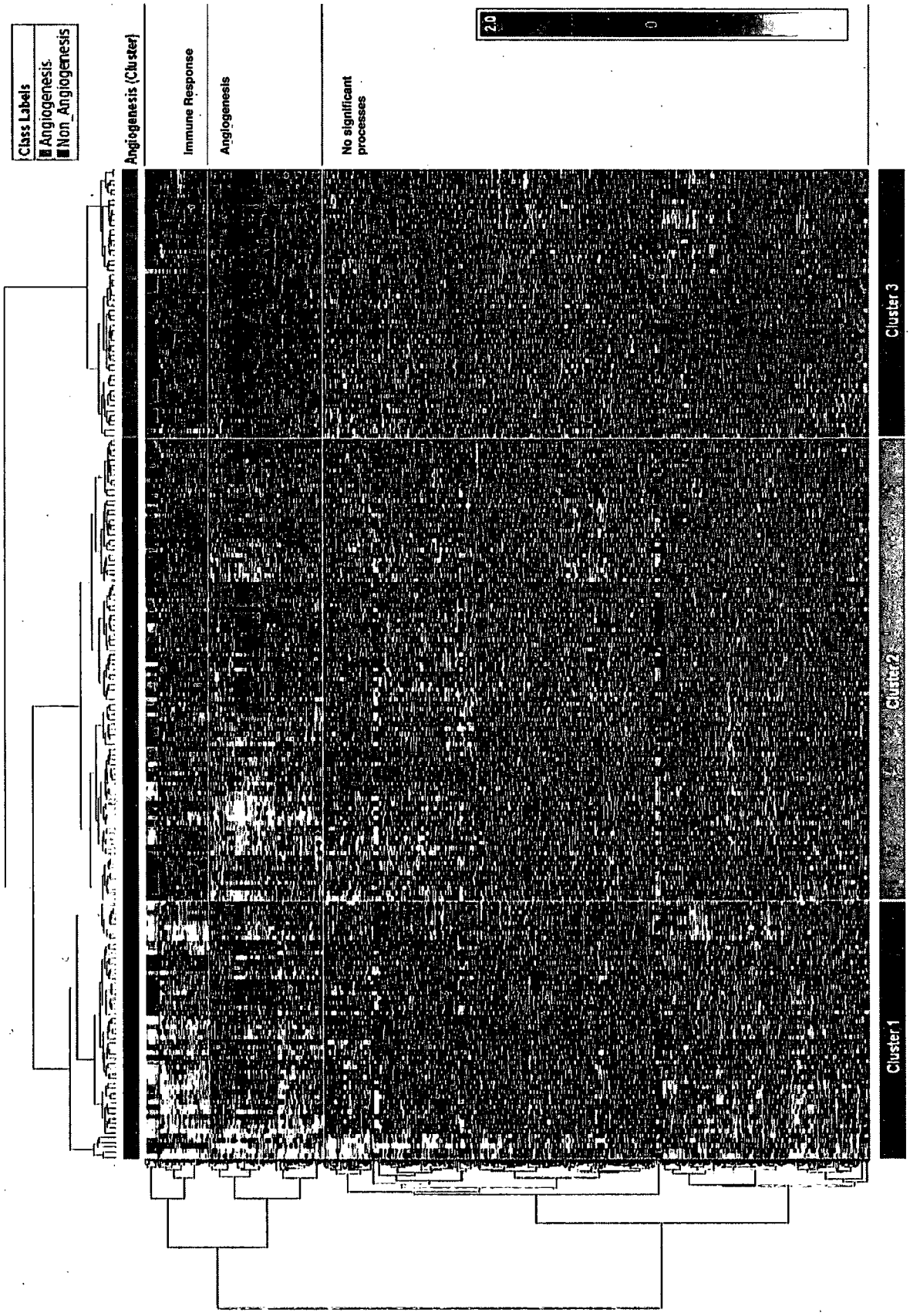

Class Labels
Angiogenesis
Non_Angiogenesis
Angiogenesis (Cluster)
Immune Response
Angiogenesis
No significant processes
2.0
0
Cluster 3
Cluster 2
Cluster 1

Figure 16

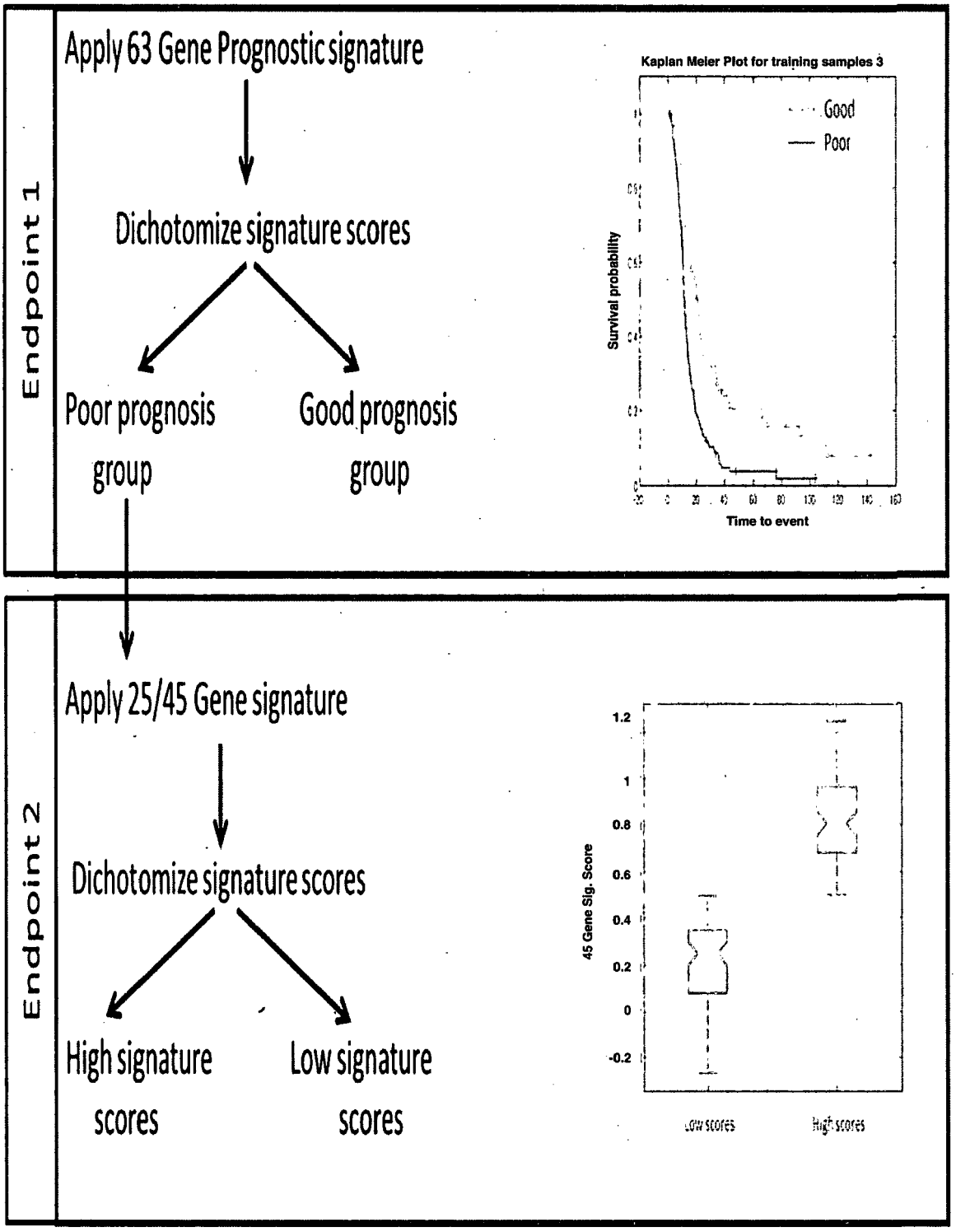
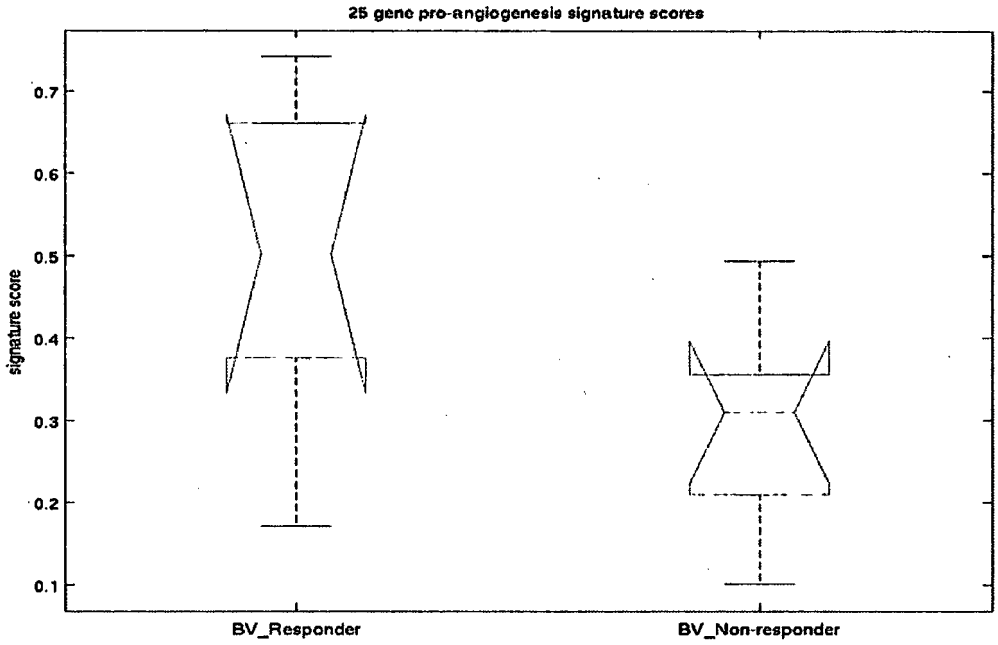

Endpoint 1
Apply 63 Gene Prognostic signature
Dichotomize signature scores
Poor prognosis group
Good prognosis group
Kaplan Meier Plot for training samples 3
Good
Poor
Survival probability
Time to event
Endpoint 2
Apply 25/45 Gene signature
Dichotomize signature scores
High signature scores
Low signature scores
45 Gene Sig. Score
1.2
1
0.8
0.6
0.4
0.2
0
-0.2
Low scores
High scores

Figure 17

A


25 gene pro-angiogenesis signature scores
signature score
0.7
0.6
0.5
0.4
0.3
0.2
0.1
BV_Responder
BV_Non-responder

B

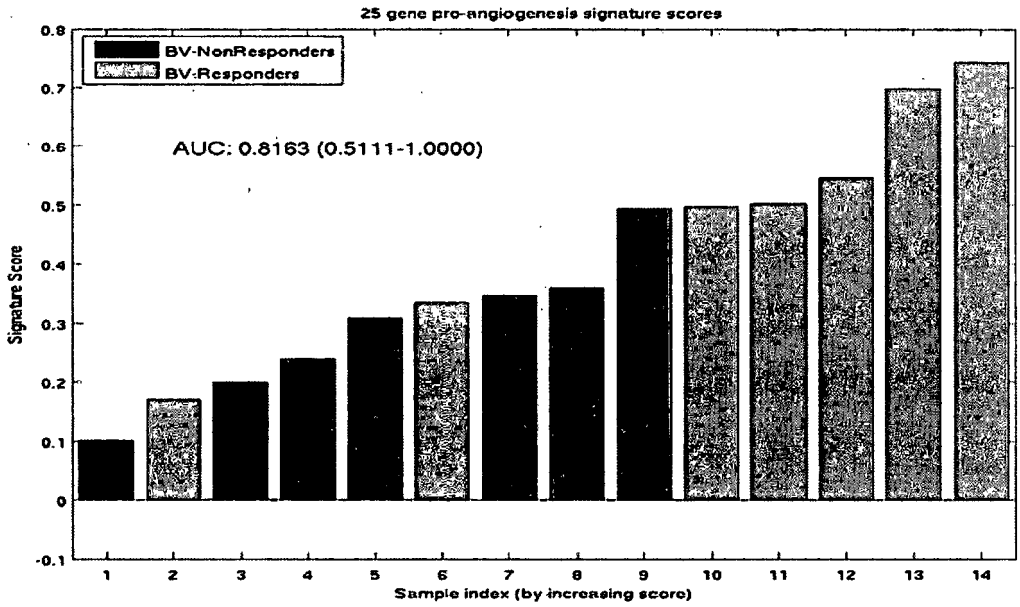
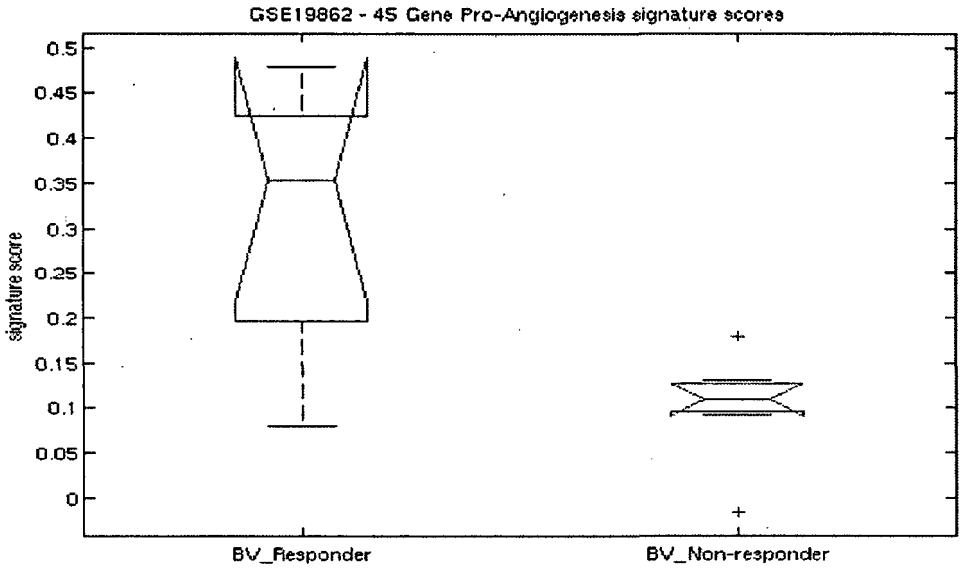

25 gene pro-angiogenesis signature scores
BV-NonResponders
BV-Responders
AUC: 0.8163 (0.5111-1.0000)
Signature Score
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
1
2
3
4
5
6
7
8
9
10
11
12
13
14
Sample index (by increasing score)

Figure 18

A


GSE19862 - 45 Gene Pro-Angiogenesis signature scores
signature score
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
BV_Responder
BV_Non-responder

B

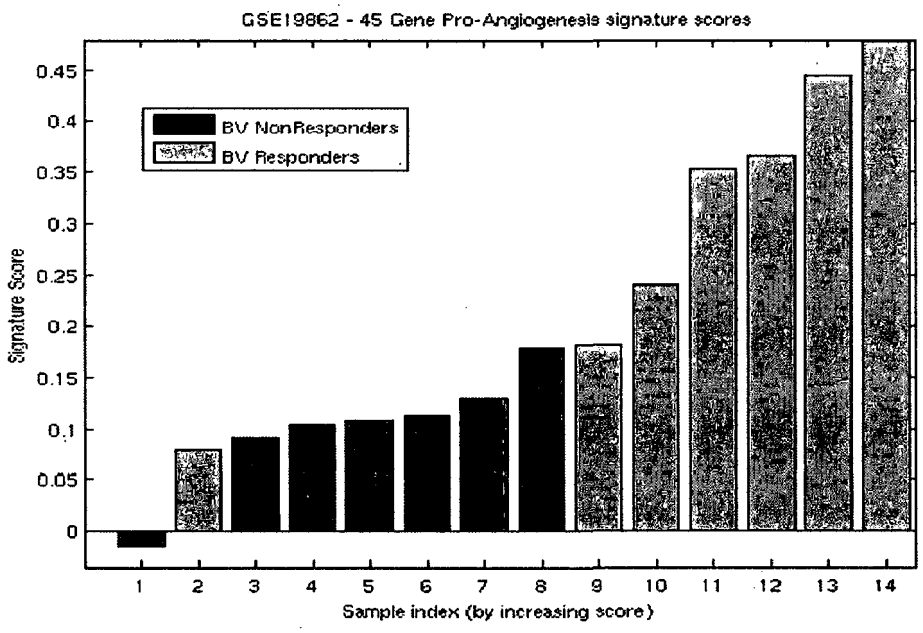

GSE19862 - 45 Gene Pro-Angiogenesis signature scores
BV NonResponders
BV Responders
Signature Score
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
Sample index (by increasing score)

Figure 19