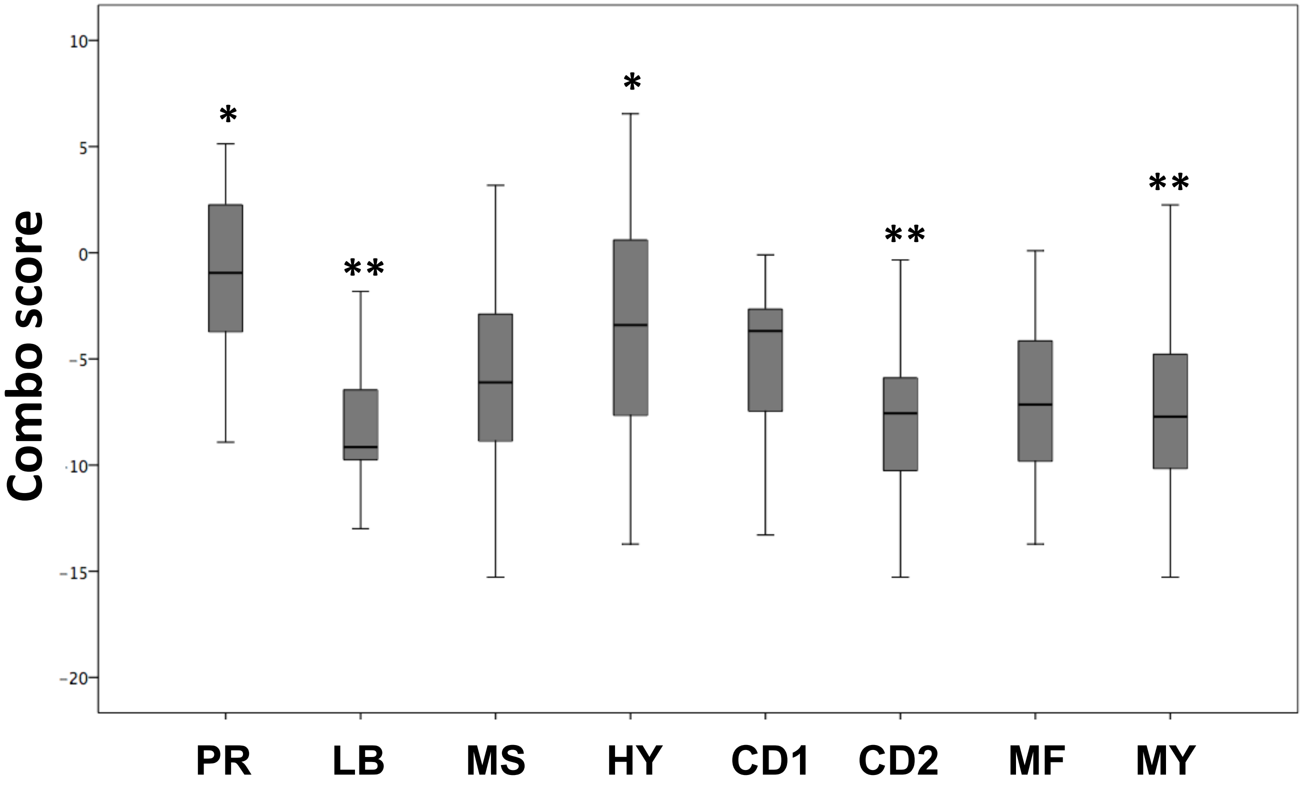
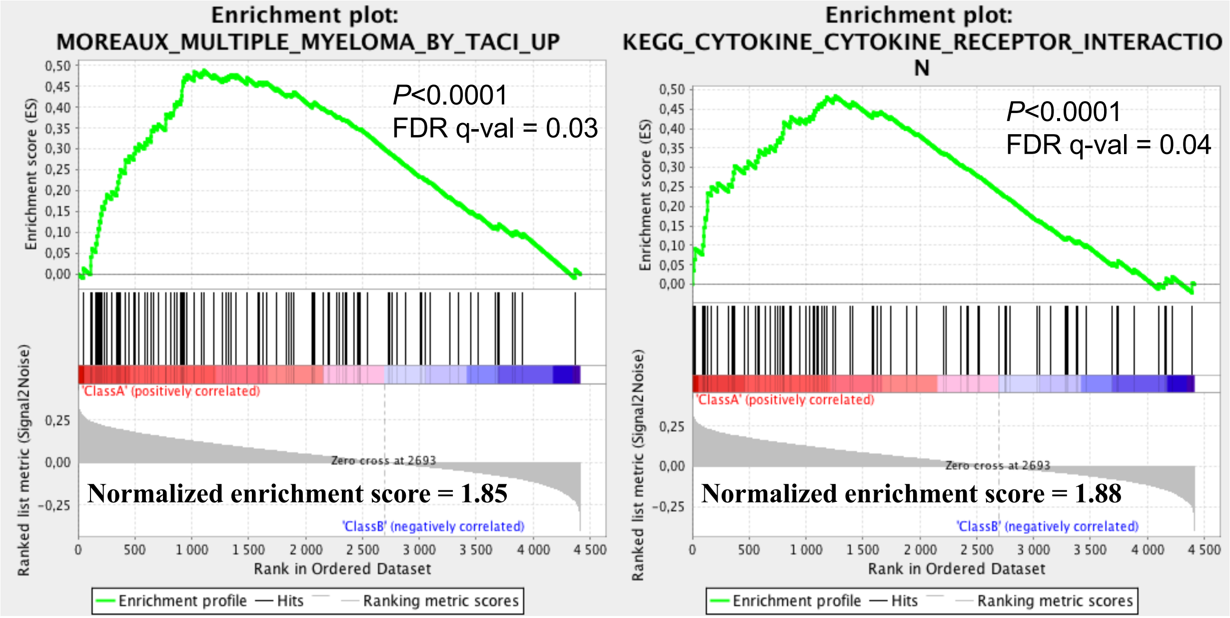
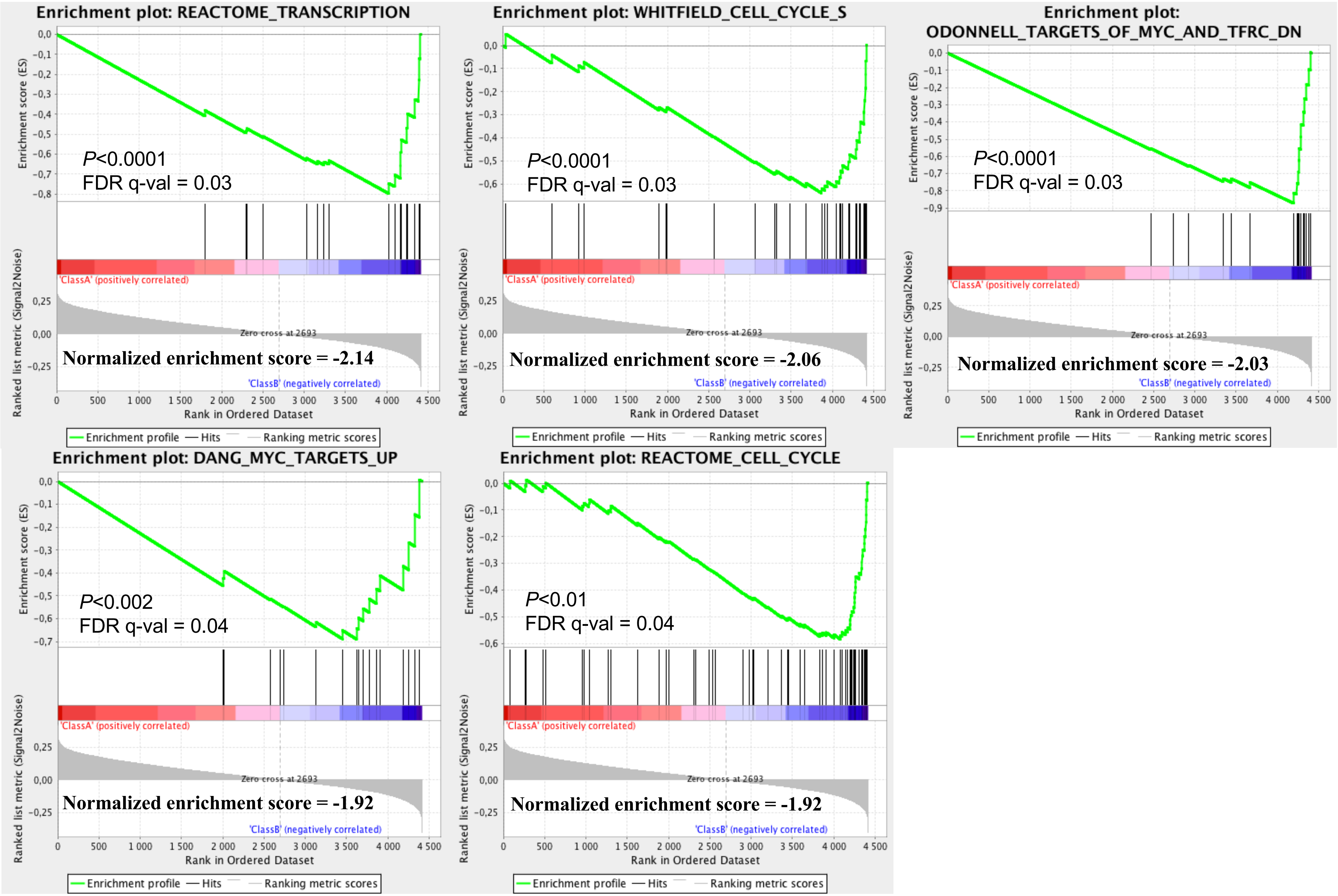


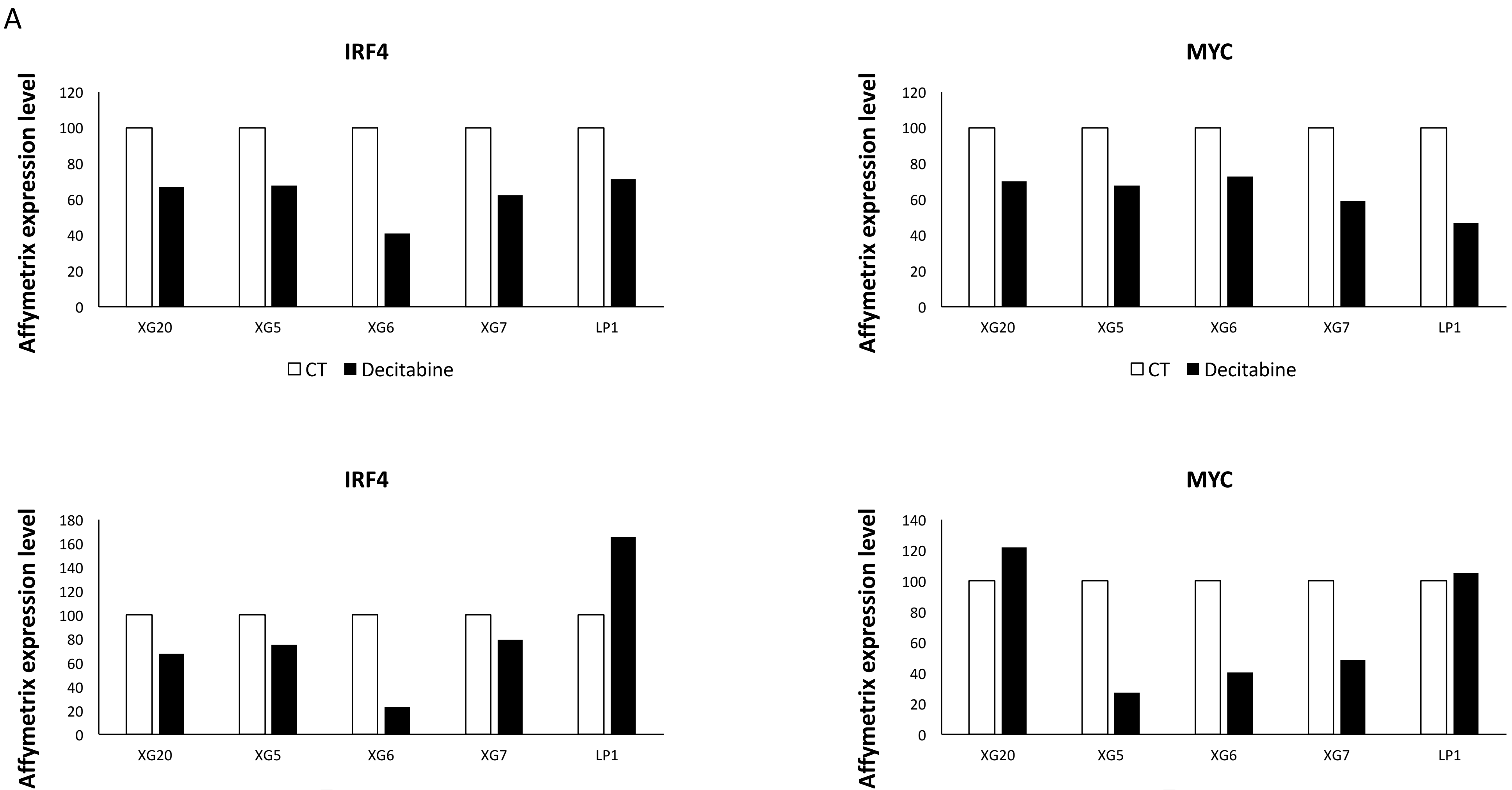
Supplementary Figure S1: The Combo score was computed for MMCs of patients belonging to the 8 groups of the UAMS molecular classification of multiple myeloma, using UAMS-TT2 cohort. PR: proliferation, LB: low bone disease, MS: MMSET, HY: hyperdiploid, CD1: Cyclin D1-D3, CD2: Cyclin D1-D3, MF: MAF, MY: myeloid. * Indicate that the score value is significantly higher in the group compared to all the patients of the cohort ($P < .05$). ** Indicate that the score value is significantly lower in the group compared to all the patients of the cohort ($P < .05$).

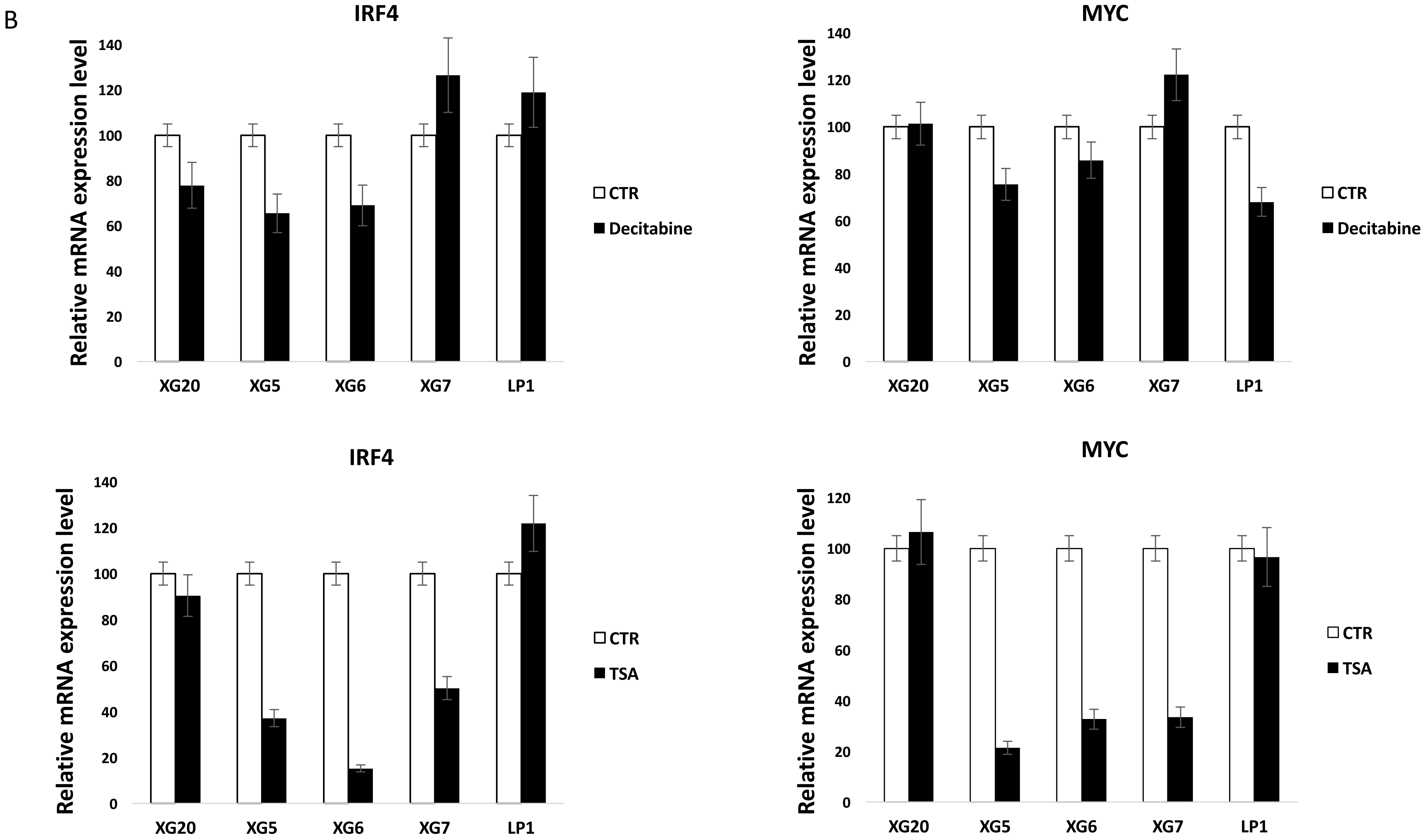


Supplementary Figure S2. Top gene set significantly associated with low Combo Score in MM. GSEA enrichment plot with the absolute enrichment p value and the normalized enrichment score of the gene set.

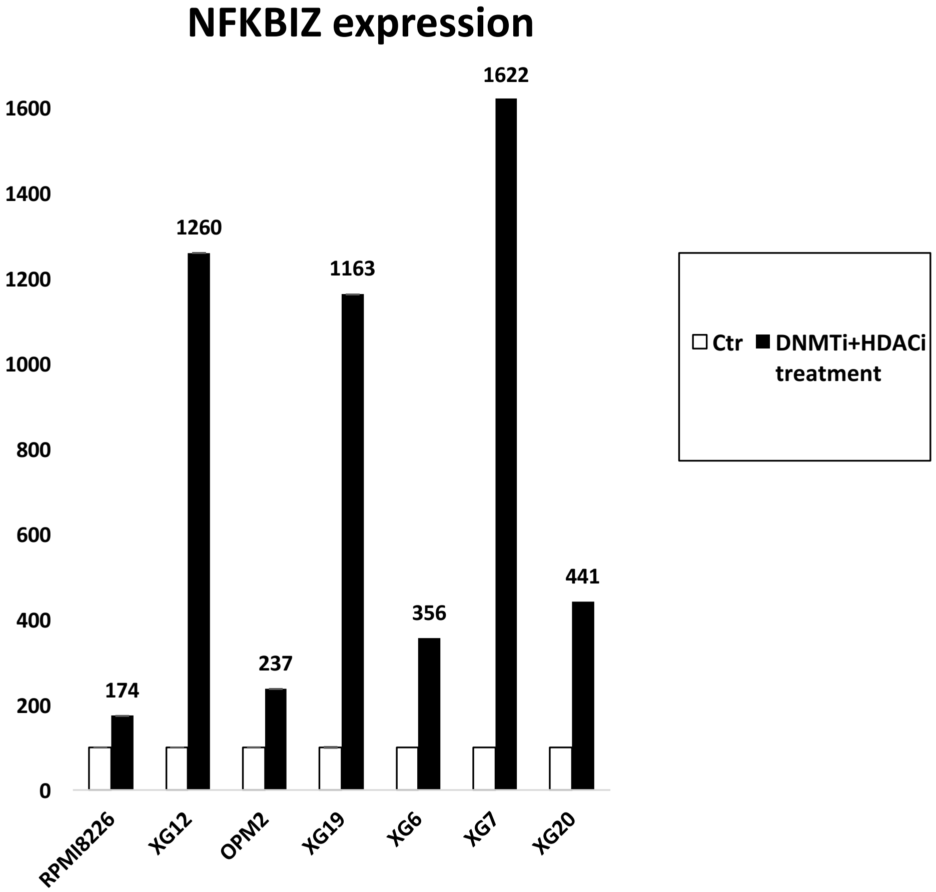

Enrichment plot: REACTOME_TRANSCRIPTION
P<0.0001
FDR q-val = 0.03
Normalized enrichment score = -2.14
Enrichment plot: WHITFIELD_CELL_CYCLE_S
P<0.0001
FDR q-val = 0.03
Normalized enrichment score = -2.06
Enrichment plot: ODONNELL_TARGETS_OF_MYC_AND_TFRC_DN
P<0.0001
FDR q-val = 0.03
Normalized enrichment score = -2.03
Enrichment plot: DANG_MYC_TARGETS_UP
P<0.002
FDR q-val = 0.04
Normalized enrichment score = -1.92
Enrichment plot: REACTOME_CELL_CYCLE
P<0.01
FDR q-val = 0.04
Normalized enrichment score = -1.92
Enrichment score (ES)
Ranked list metric (Signal2Noise)
'ClassA' (positively correlated)
'ClassB' (negatively correlated)
Zero cross at 2693
Rank in Ordered Dataset
0
500
1 000
1 500
2 000
2 500
3 000
3 500
4 000
4 500
0,25
0,00
-0,25
Enrichment profile
Hits
Ranking metric scores

Supplementary Figure S3. Top gene set significantly associated with high Combo Score in MM. GSEA enrichment plot with the absolute enrichment p value and the normalized enrichment score of the gene set.


A
IRF4
MYC
Affymetrix expression level
0
20
40
60
80
100
120
140
160
180
XG20
XG5
XG6
XG7
LP1
□ CT ■ Decitabine
□ CT ■ TSA


B
IRF4
Relative mRNA expression level
0
20
40
60
80
100
120
140
XG20
XG5
XG6
XG7
LP1
CTR
Decitabine
MYC
Relative mRNA expression level
0
20
40
60
80
100
120
140
XG20
XG5
XG6
XG7
LP1
CTR
Decitabine
IRF4
Relative mRNA expression level
0
20
40
60
80
100
120
140
XG20
XG5
XG6
XG7
LP1
CTR
TSA
MYC
Relative mRNA expression level
0
20
40
60
80
100
120
XG20
XG5
XG6
XG7
LP1
CTR
TSA

Supplementary Figure S4. *IRF4* and *MYC* gene expression in untrated (CT) and DNMTi or HDACi treated HMCLs using Affymetrix microarrays (A) and real time PCR (B).



Supplementary Figure S5. *NFKBIZ* gene expression in untreated (CT) and DNMTi/HDACi treated HMCLs was assayed using real time PCR.