Additional Methods

Self-identified genes

Apart from 4 gene sets derived from previous classifiers, we also identified a new gene set based on both GSE4732_p1 and GSE4475. And we only considered the high confidence samples in the previous classifiers to identify differentially expressed genes between BL and DLBCL. In the Dave classifier (GSE4732_p1), we compared against the consistent 44 BL versus 235 DLBCL agreed by both pathological and molecular diagnosis; and in the Hummel classifier (GSE4475) we only compared the 44 mBLs against the 129 non-mBLs. First 100 most significantly differentially expressed genes between the two groups in each data set were selected by limma package, and there are 54 genes overlap. The new identified gene set was consist of the 54 overlap genes with 6 genes that applied in both two previous classifiers but not picked in above selecting method.

Quality Control of Clinical FFPE samples

Quality check involved the detected signal over all probes, housekeeping control probes, annealing control probes, cyc_hyb control probes, low stringency control probes and negative control probes. Arrays falling beyond 1.645 standard deviations from the mean of a criterion were considered failures at that criterion, and arrays were removed from the data set if they failed at probe detection or housekeeping genes or either two of annealing control probes, cyc_hyb control probes, low stringency control probes or negative control probes. And there are 97 and 119 samples removed from downstream analysis due to poor quality in Version 3 and Version 4 dataset respectively.

Supplementary Tables

Supplementary Table 1: Accuracy of 10-fold cross-validation in two data sets

	GSE4732(1): Multi-Class	GSE4475: Multi-Class	GSE4732(1): Binary-Class	GSE4475: Strict	GSE4475: Wide	Average
LibSVM	88.45	91.86	99.01	98.19	96.39	94.78
SMO	88.45	92.77	98.68	97.74	95.03	94.534
MultilayerPerceptron	89.11	89.6	98.68	97.29	96.39	94.214
RandomForest100	83.83	93.22	98.35	98.19	96.39	93.996
FT	86.47	88.24	98.35	97.74	93.67	92.894
LMT	82.51	86.88	99.01	97.29	94.57	92.052
BayesNet	77.23	89.6	97.7	97.74	95.93	91.64
NaiveBayes	77.56	88.24	98.35	97.74	95.48	91.474
J48	73.27	81.91	97.03	92.77	90.5	87.096
REP tree	72.3	81.91	94.72	95.48	90.96	87.074

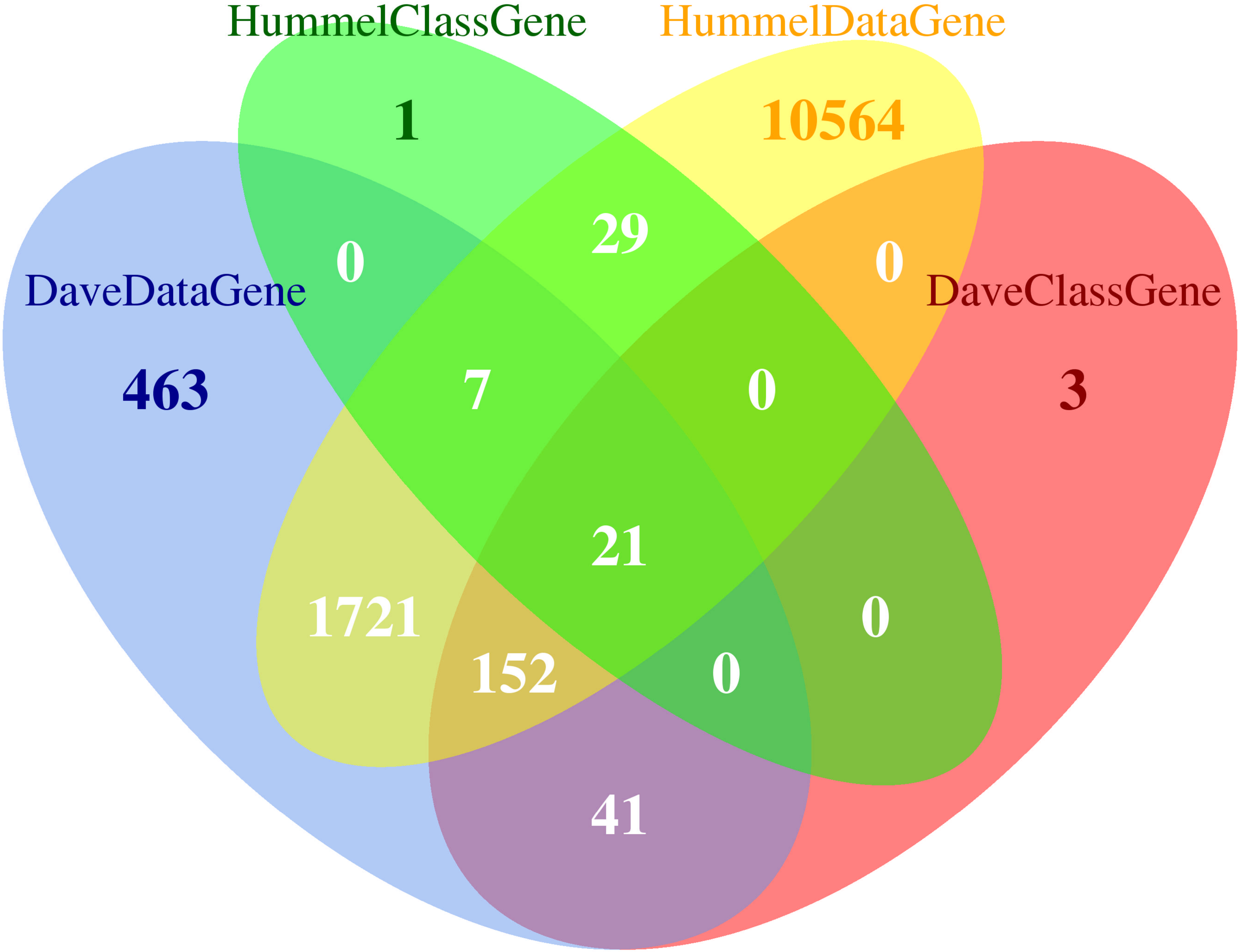
[1] GSE4732(1) Multi-Class includes 54 BL, 91 ABC (Activated B-Cell-like), 95 GCB (Germinal Centre B-cell-like), 33 PMBL (Primary Mediastinal B-cell Lymphoma), 30 Unclassified DLBCL, ; GSE4732(1) Binary-Class are 54 BL and 249 DLBCLs.

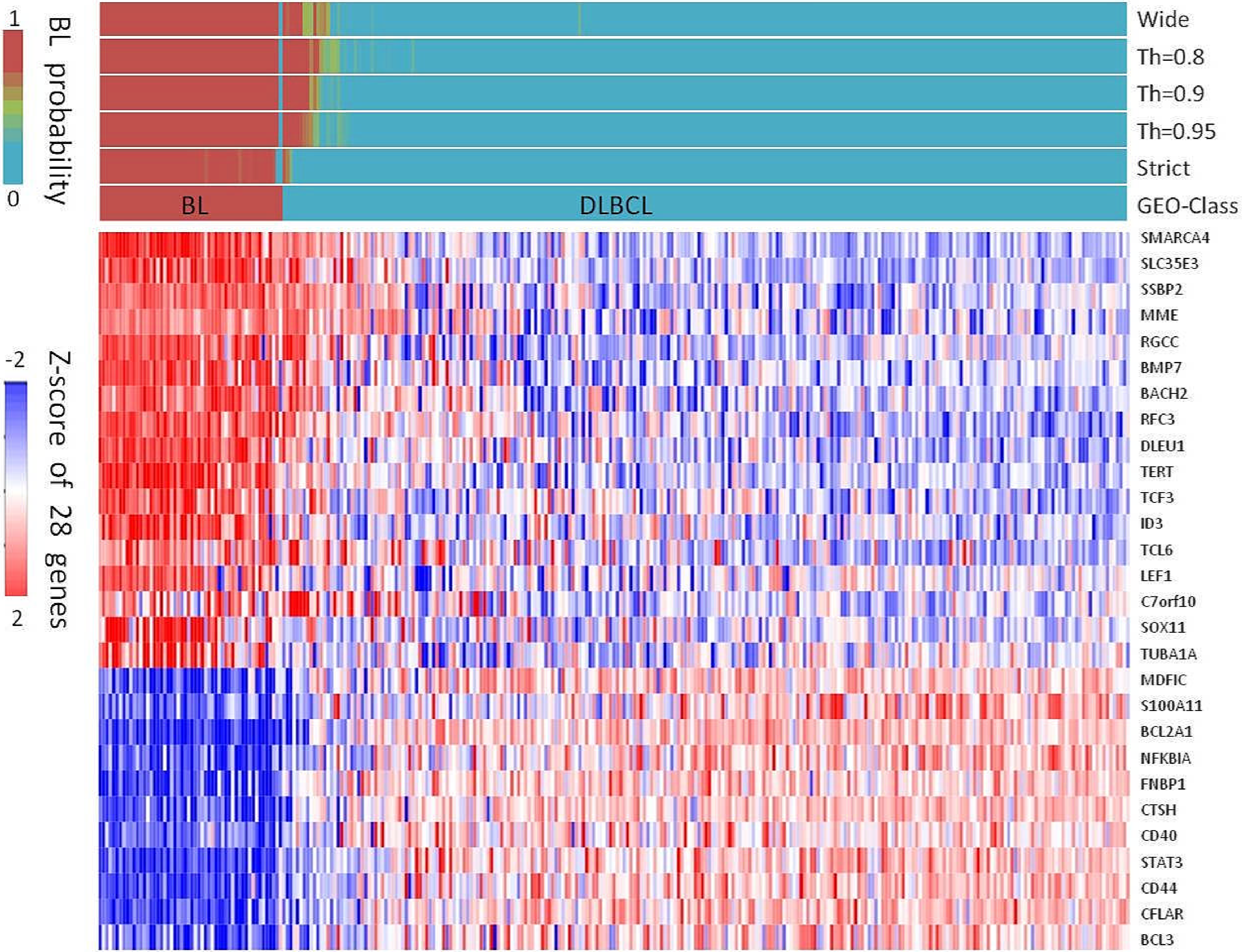
[2] GSE4475 Multi-Class are 44 mBL, 48 intermediate and 129 non-mBL cases; GSE4475 strict are 44 BL versus 177 others; GSE4475 wide are 59 BL and 162 DLBCL divided by author assigned BL probability equals 0.5

Supplementary Table 2: Overall accuracy of tested gene lists in building the classifier

	GSE4732 default	GSE4475strict default	GSE4475wide default	GSE4732 optimized	GSE4475strict optimized	GSE4475wide optimized	Average
original-gene	0.99	0.977	0.959	0.993	0.986	0.977	0.980
10-gene	0.974	0.968	0.954	0.97	0.968	0.955	0.965
21-gene	0.977	0.968	0.95	0.99	0.977	0.955	0.969
28-gene	0.984	0.977	0.954	0.993	0.982	0.955	0.974
60-gene	0.98	0.977	0.936	0.99	0.977	0.955	0.969
172-gene	0.984	0.973	0.945	0.99	0.977	0.955	0.971

*only 6 of the 10 NanoGene are found and tested in GSE4732(1) dataset


HummelClassGene
HummelDataGene
DaveDataGene
DaveClassGene
1
10564
29
0
0
463
7
0
3
21
1721
0
152
0
41


1
BL probability
0
Wide
Th=0.8
Th=0.9
Th=0.95
Strict
BL
DLBCL
GEO-Class
-2
Z-score of 28 genes
2
SMARCA4
SLC35E3
SSBP2
MME
RGCC
BMP7
BACH2
RFC3
DLEU1
TERT
TCF3
ID3
TCL6
LEF1
C7orf10
SOX11
TUBA1A
MDFIC
S100A11
BCL2A1
NFKBIA
FNBP1
CTSH
CD40
STAT3
CD44
CFLAR
BCL3