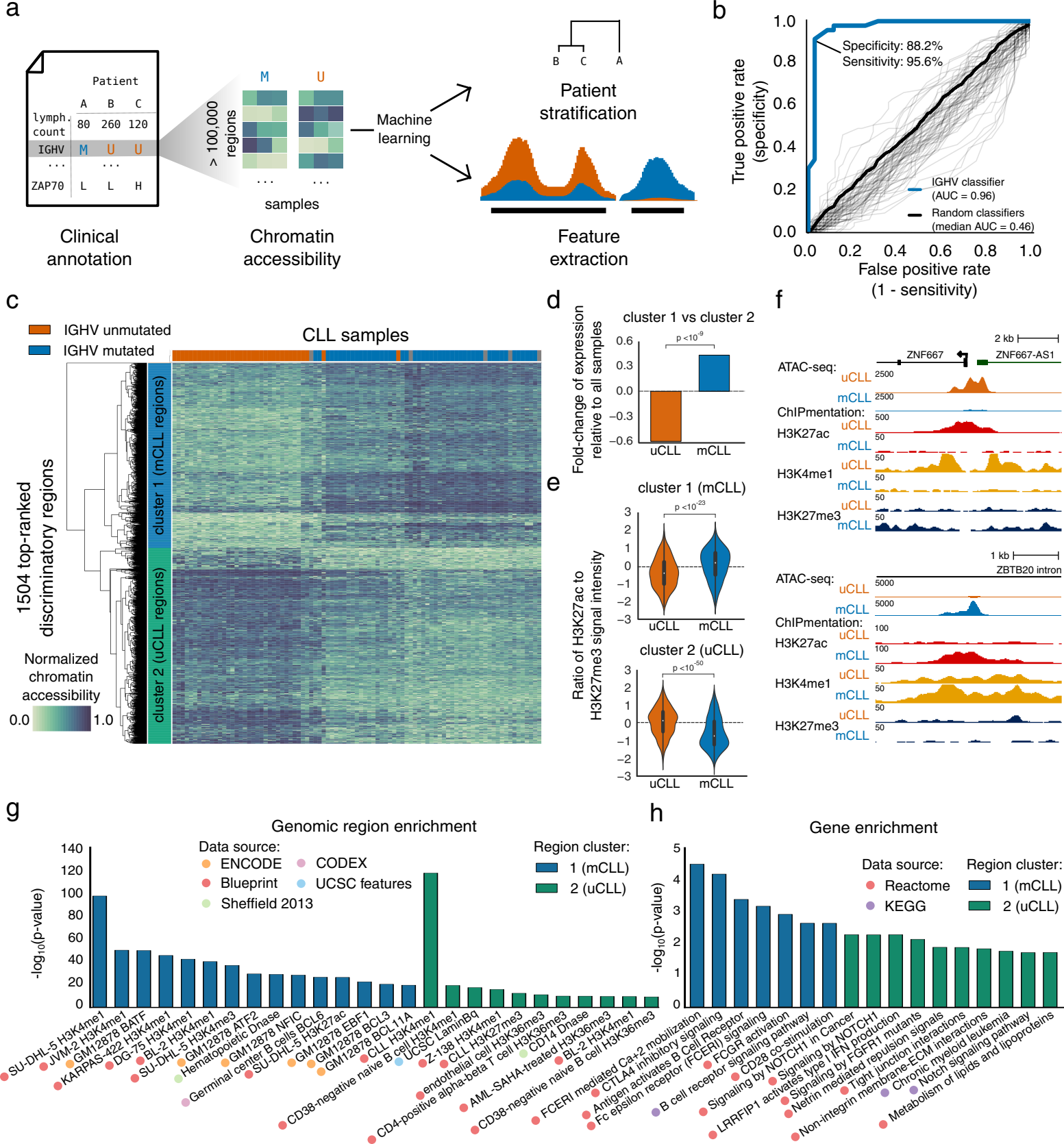
a
Patient
A B C
lymph. count 80 260 120
IGHV M U U
ZAP70 L L H
> 100,000 regions
M U
samples
Machine learning
B C A
Patient stratification
Clinical annotation
Chromatin accessibility
Feature extraction
b
Specificity: 88.2%
Sensitivity: 95.6%
IGHV classifier (AUC = 0.96)
Random classifiers (median AUC = 0.46)
True positive rate (specificity)
False positive rate (1 - sensitivity)
c
IGHV unmutated
IGHV mutated
CLL samples
1504 top-ranked discriminatory regions
cluster 1 (mCLL regions)
cluster 2 (uCLL regions)
Normalized chromatin accessibility
0.0 1.0
d
cluster 1 vs cluster 2
Fold-change of expression relative to all samples
p <10^-9
uCLL mCLL
e
cluster 1 (mCLL)
p <10^-23
cluster 2 (uCLL)
p <10^-50
Ratio of H3K27ac to H3K27me3 signal intensity
f
ZNF667 ZNF667-AS1
2 kb
ATAC-seq:
ChIPmentation:
H3K27ac
H3K4me1
H3K27me3
uCLL mCLL
ZBTB20 intron
1 kb
g
Genomic region enrichment
Data source:
ENCODE
Blueprint
Sheffield 2013
CODEX
UCSC features
Region cluster:
1 (mCLL)
2 (uCLL)
-log10(p-value)
SU-DHL-5 H3K4me1
JVM-2 H3K4me1
GM12878 BATF
KARPAS-422 H3K4me1
DG-75 H3K4me1
BL-2 H3K4me1
SU-DHL-5 H3K4me3
GM12878 ATF2
Hematopoietic Dnase
GM12878 NFIC
Germinal center B cells BCL6
SU-DHL-5 H3K27ac
GM12878 EBF1
GM12878 BCL3
GM12878 BCL11A
CLL H3K4me1
UCSC LaminBq
Z-138 H3K4me1
CLL H3K27me3
endothelial cell H3K36me3
CD14 Dnase
AML-SAHA-treated H3K36me3
CD38-negative naive B cell H3K36me3
BL-2 H3K4me1
FCERI mediated Ca+2 mobilization
CTLA4 inhibitory signaling
Antigen activates B Cell Receptor
Fc epsilon receptor (FCERI) signaling
FCGR activation
B cell receptor signaling pathway
CD28 co-stimulation
Signaling by NOTCH1 in Cancer
Signaling by NOTCH1
LRRFIP1 activates type I IFN production
Signaling by FGFR1 mutants
Netrin mediated repulsion signals
Tight junction interactions
Non-integrin membrane-ECM interactions
Chronic myeloid leukemia
Notch signaling pathway
Metabolism of lipids and lipoproteins
h
Gene enrichment
Data source:
Reactome
KEGG
Region cluster:
1 (mCLL)
2 (uCLL)
-log10(p-value)