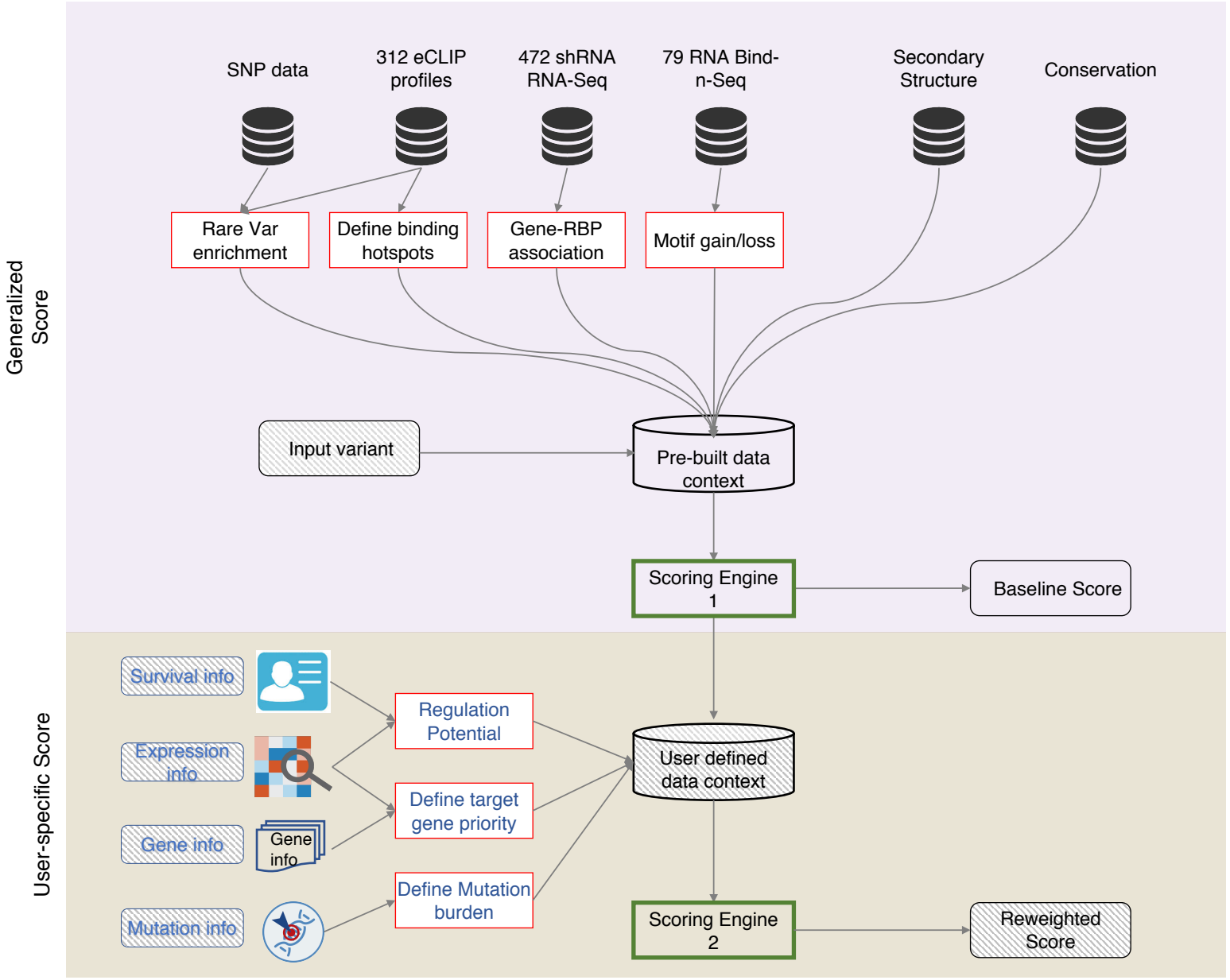
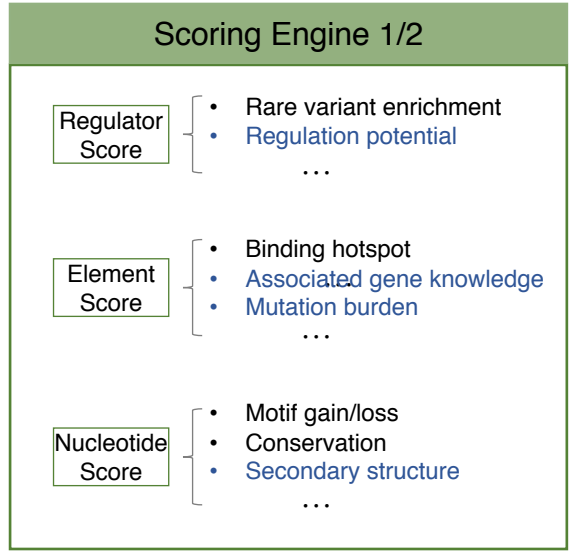
Figure 1


Generalized Score
SNP data
312 eCLIP profiles
472 shRNA RNA-Seq
79 RNA Bind-n-Seq
Secondary Structure
Conservation
Rare Var enrichment
Define binding hotspots
Gene-RBP association
Motif gain/loss
Input variant
Pre-built data context
Scoring Engine 1
Baseline Score
User-specific Score
Survival info
Expression info
Gene info
Mutation info
Gene info
Regulation Potential
Define target gene priority
Define Mutation burden
User defined data context
Scoring Engine 2
Reweighted Score


Scoring Engine 1/2
Regulator Score
Rare variant enrichment
Regulation potential
...
Element Score
Binding hotspot
Associated gene knowledge
Mutation burden
...
Nucleotide Score
Motif gain/loss
Conservation
Secondary structure
...

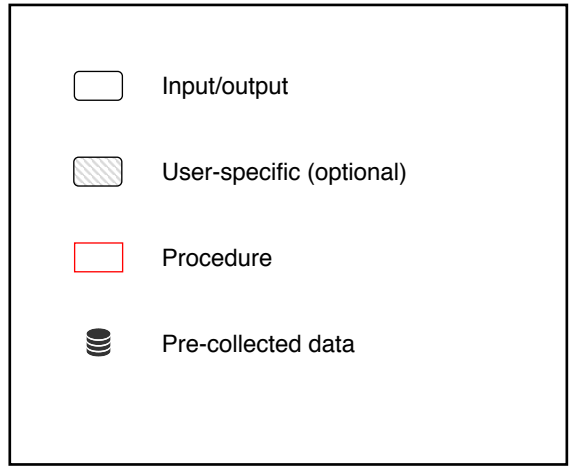

Input/output
User-specific (optional)
Procedure
Pre-collected data

Figure 2

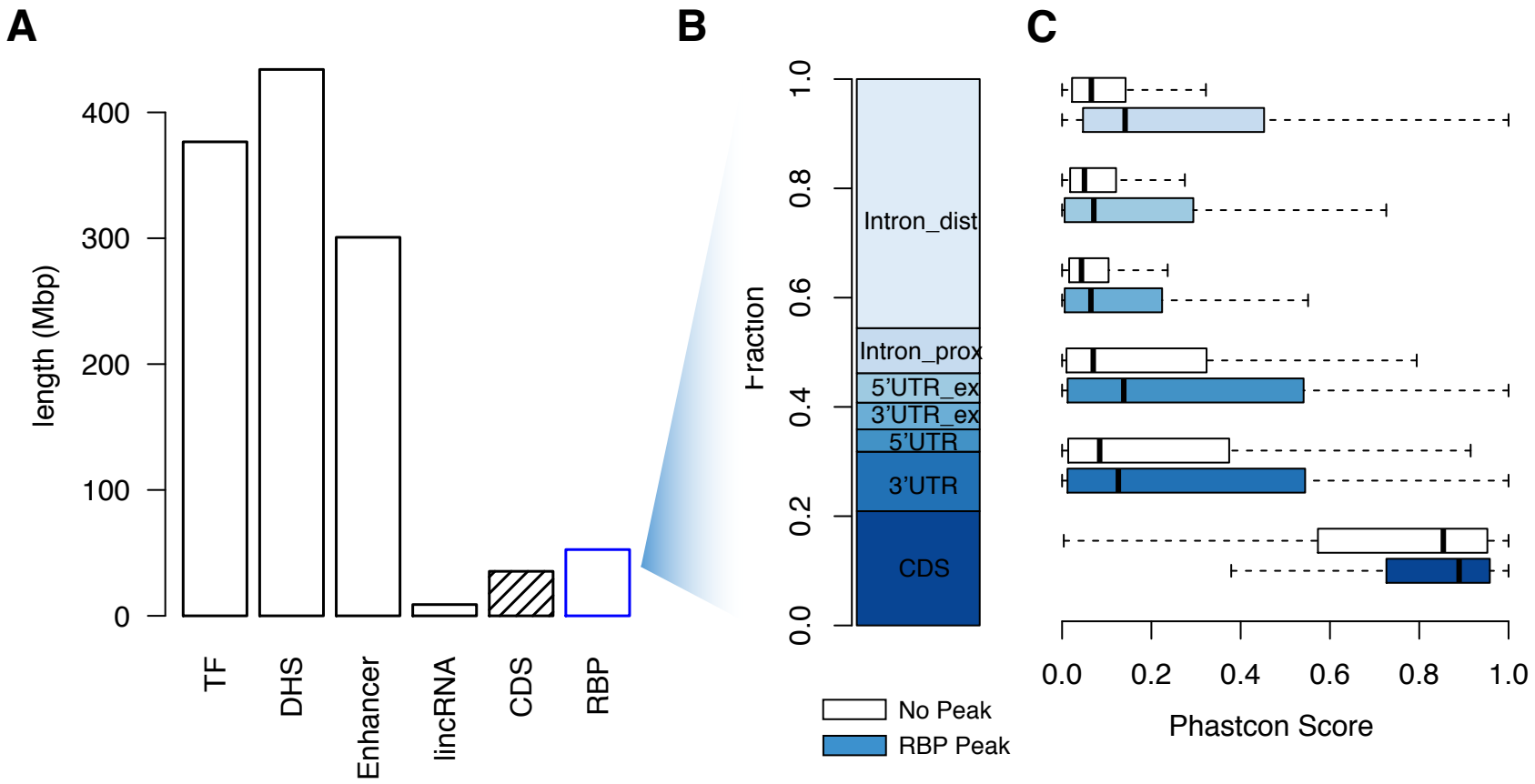

A
length (Mbp)
400
300
200
100
0
TF
DHS
Enhancer
lincRNA
CDS
RBP
B
Fraction
1.0
0.8
0.6
0.4
0.2
0.0
Intron_dist
Intron_prox
5'UTR_ex
3'UTR_ex
5'UTR
3'UTR
CDS
No Peak
RBP Peak
C
0.0
0.2
0.4
0.6
0.8
1.0
Phastcon Score

Figure 3

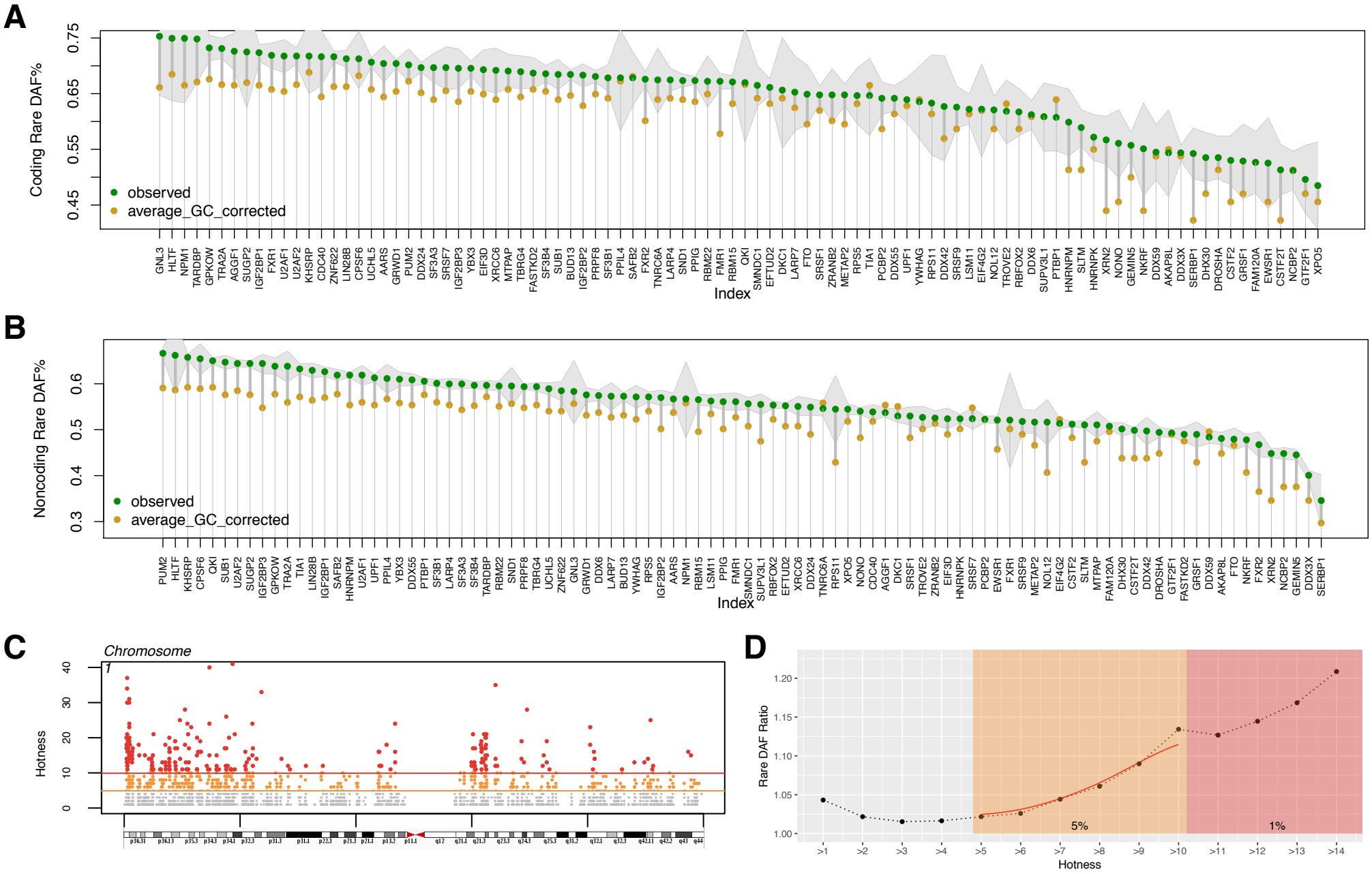
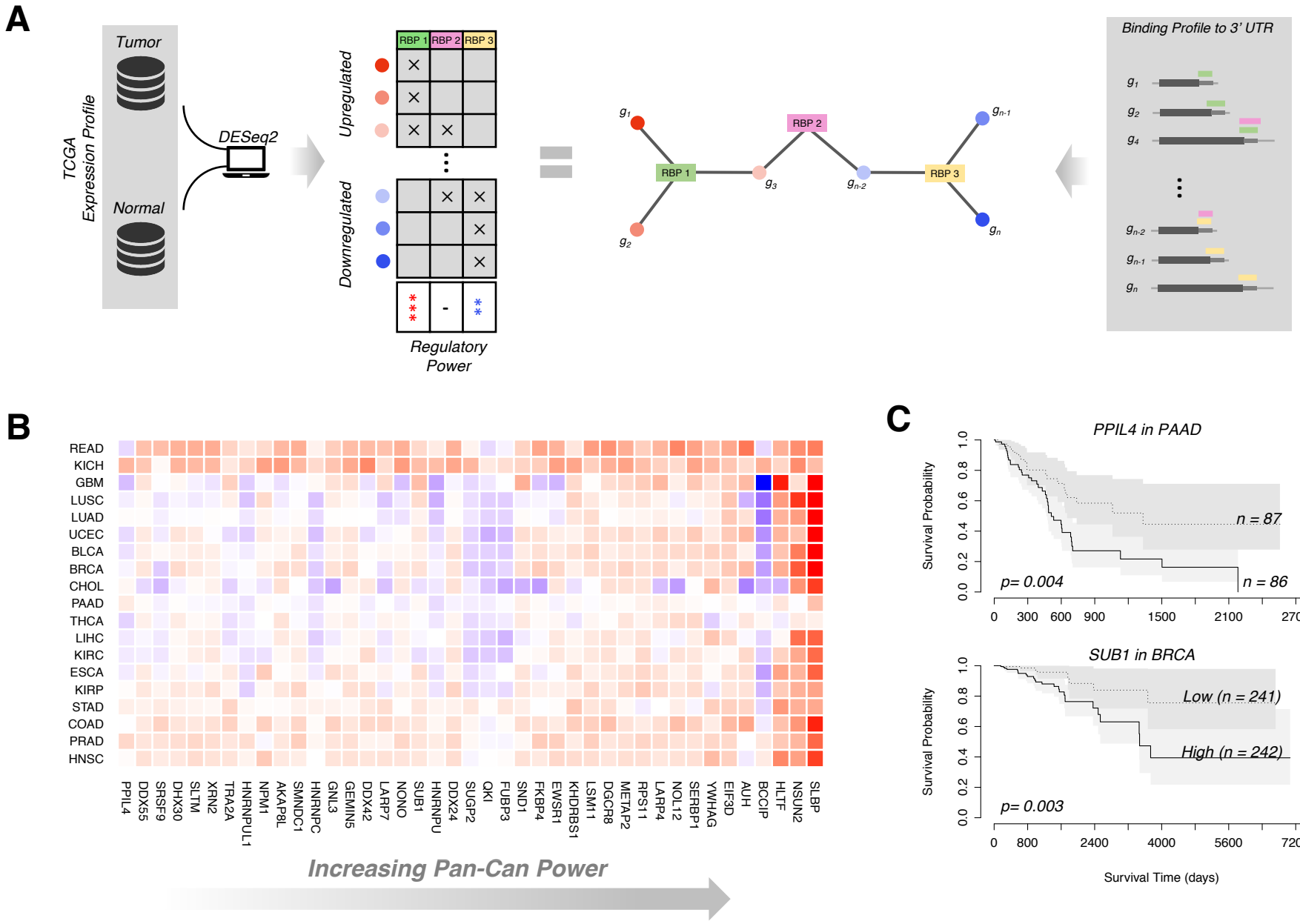
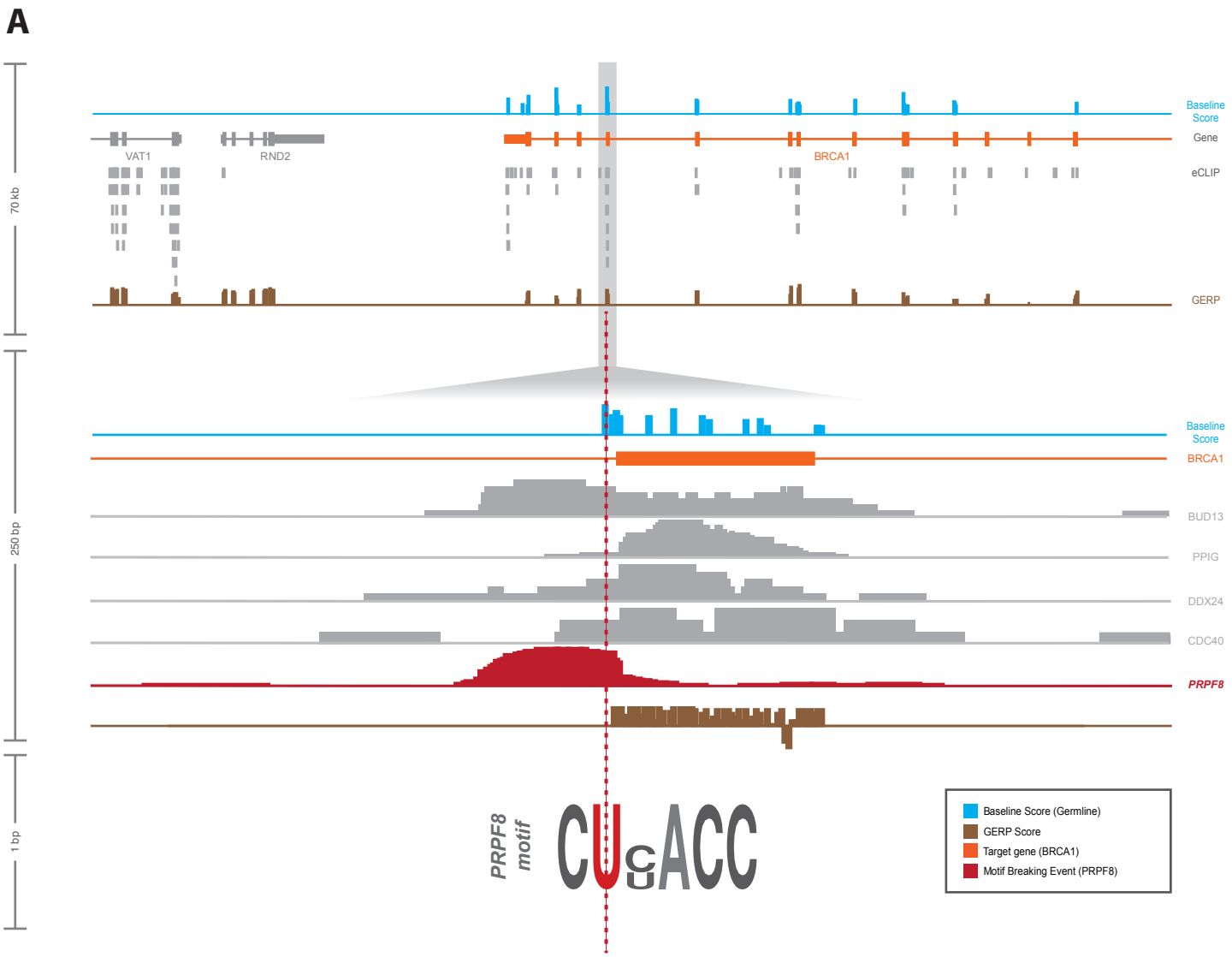
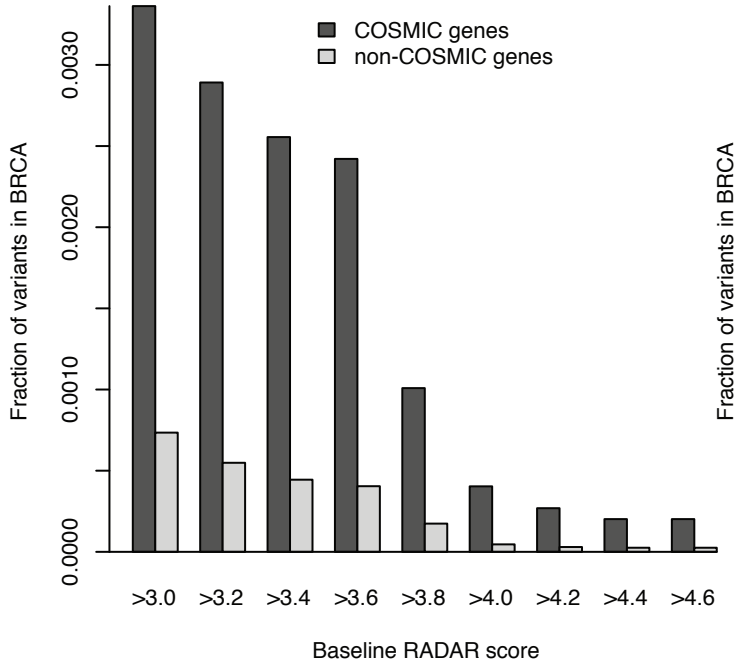
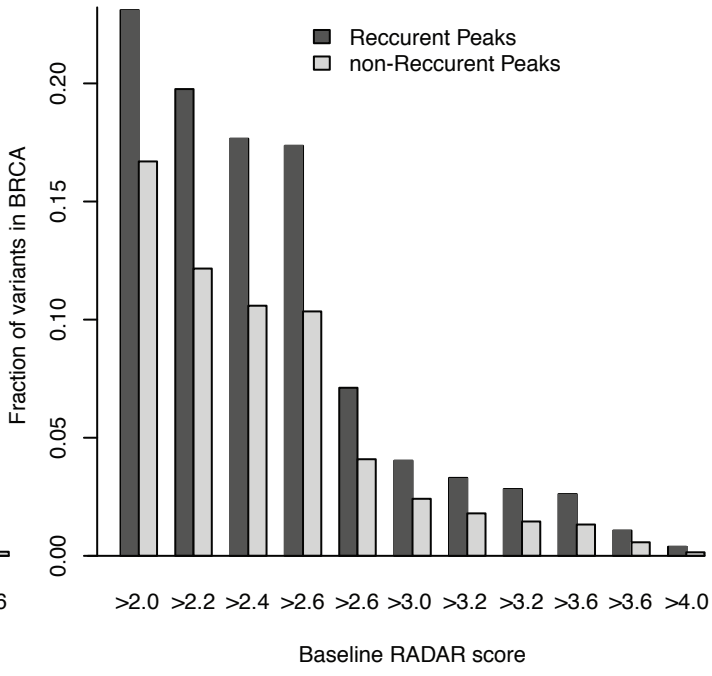

A
Coding Rare DAF%
0.45
0.55
0.65
0.75
observed
average_GC_corrected
GNL3 HLTF NPM1 TARDBP GPKOW TRA2A AGGF1 SUGP2 IGF2BP1 FXR1 U2AF1 U2AF2 KHSRP CDC40 ZNF622 LIN28B CPSF6 UCHL5 AARS GRWD1 PUM2 DDX24 SF3A3 SRSF7 IGF2BP3 YBX3 EIF3D XRCC6 MTPAP TBRG4 FASTKD2 SF3B4 SUB1 BUD13 IGF2BP2 PRPF8 SF3B1 PPIL4 SAFB2 FXR2 TNRC6A LARP4 SND1 PPIG RBM22 FMR1 RBM15 QKI SMNDC1 EFTUD2 DKC1 LARP7 FTO SRSF1 ZRANB2 METAP2 RPS5 TIA1 PCBP2 DDX55 UPF1 YWHAG RPS11 DDX42 SRSF9 LSM11 EIF4G2 NOL12 TROVE2 RBFOX2 DDX6 SUPV3L1 PTBP1 HNRNPM SLTM HNRNPK XRN2 NONO GEMIN5 NKRF DDX59 AKAP8L DDX3X SERBP1 DHX30 DROSHA CSTF2 GRSF1 FAM120A EWSR1 CSTF2T NCBP2 GTF2F1 XPO5
Index
B
Noncoding Rare DAF%
0.3
0.4
0.5
0.6
observed
average_GC_corrected
PUM2 HLTF KHSRP CPSF6 QKI SUB1 U2AF2 SUGP2 IGF2BP3 GPKOW TRA2A TIA1 LIN28B IGF2BP1 SAFB2 HNRNPM U2AF1 UPF1 PPIL4 YBX3 DDX55 PTBP1 SF3B1 LARP4 SF3A3 SF3B4 TARDBP RBM22 SND1 PRPF8 TBRG4 UCHL5 ZNF622 GNL3 GRWD1 DDX6 LARP7 BUD13 YWHAG RPS5 IGF2BP2 AARS NPM1 RBM15 LSM11 PPIG FMR1 SMNDC1 SUPV3L1 RBFOX2 EFTUD2 XRCC6 DDX24 TNRC6A RPS11 XPO5 NONO CDC40 AGGF1 DKC1 SRSF1 TROVE2 ZRANB2 EIF3D HNRNPK SRSF7 PCBP2 EWSR1 FXR1 SRSF9 METAP2 NOL12 EIF4G2 CSTF2 SLTM MTPAP FAM120A DHX30 CSTF2T DDX42 DROSHA GTF2F1 FASTKD2 GRSF1 DDX59 AKAP8L FTO NKRF FXR2 XRN2 NCBP2 GEMIN5 DDX3X SERBP1
Index
C
Chromosome
1
Hotness
0
10
20
30
40
D
Rare DAF Ratio
1.00
1.05
1.10
1.15
1.20
5%
1%
>1 >2 >3 >4 >5 >6 >7 >8 >9 >10 >11 >12 >13 >14
Hotness

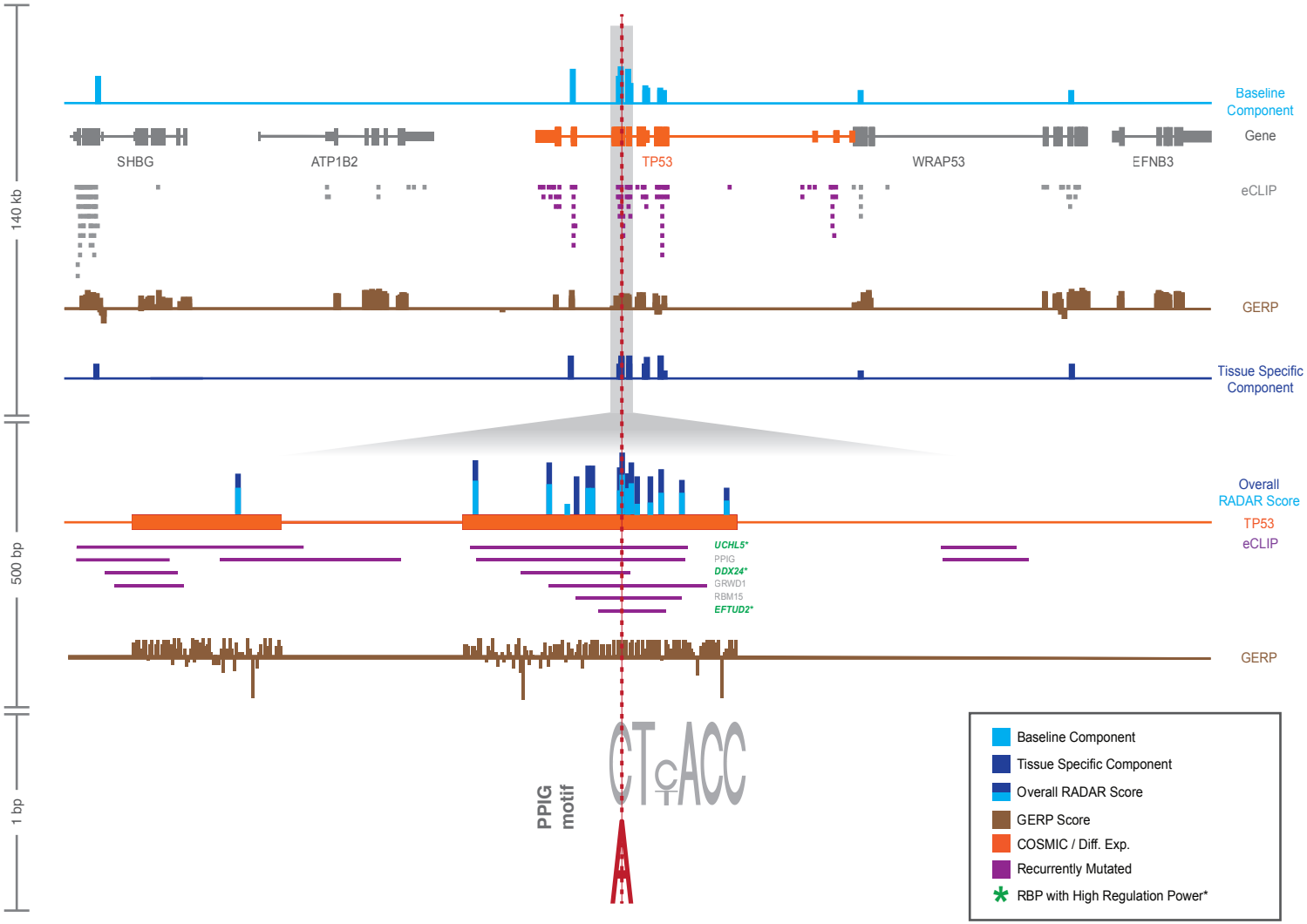
Figure 4


A
Tumor
Normal
TCGA Expression Profile
DESeq2
Upregulated
Downregulated
RBP 1
RBP 2
RBP 3
Regulatory Power
Binding Profile to 3' UTR
B
READ
KICH
GBM
LUSC
LUAD
UCEC
BLCA
BRCA
CHOL
PAAD
THCA
LIHC
KIRC
ESCA
KIRP
STAD
COAD
PRAD
HNSC
PPIL4
DDX55
SRSF9
DHX30
SLTM
XRN2
TRA2A
HNRNPUL1
NPM1
AKAP8L
SMNDC1
HNRNPC
GNL3
GEMIN5
DDX42
LARP7
NONO
SUB1
HNRNPU
DDX24
SUGP2
QKI
FUBP3
SND1
FKBP4
EWSR1
KHDRBS1
LSM11
DGCR8
METAP2
RPS11
LARP4
NOL12
SERBP1
YWHAG
EIF3D
AUH
BCCIP
HLTF
NSUN2
SLBP
Increasing Pan-Can Power
C
PPIL4 in PAAD
Survival Probability
n = 87
n = 86
p= 0.004
SUB1 in BRCA
Low (n = 241)
High (n = 242)
p= 0.003
Survival Time (days)


A
70 kb
250 bp
1 bp
VAT1
RND2
BRCA1
Baseline Score
Gene
eCLIP
GERP
BRCA1
BUD13
PPIG
DDX24
CDC40
PRPF8
PRPF8 motif
Baseline Score (Germline)
GERP Score
Target gene (BRCA1)
Motif Breaking Event (PRPF8)


B
COSMIC genes
non-COSMIC genes
Fraction of variants in BRCA
0.0000
0.0010
0.0020
0.0030
>3.0
>3.2
>3.4
>3.6
>3.8
>4.0
>4.2
>4.4
>4.6
Baseline RADAR score


C
Reccurent Peaks
non-Reccurent Peaks
Fraction of variants in BRCA
0.00
0.05
0.10
0.15
0.20
>2.0
>2.2
>2.4
>2.6
>2.6
>3.0
>3.2
>3.2
>3.6
>3.6
>4.0
Baseline RADAR score


140 kb
500 bp
1 bp
Baseline Component
Gene
SHBG
ATP1B2
TP53
WRAP53
EFNB3
eCLIP
GERP
Tissue Specific Component
Overall RADAR Score
TP53
eCLIP
UCHL5*
PPIG
DDX24*
GRWD1
RBM15
EFTUD2*
GERP
PPIG motif
Baseline Component
Tissue Specific Component
Overall RADAR Score
GERP Score
COSMIC / Diff. Exp.
Recurrently Mutated
RBP with High Regulation Power*