

Figure S1:

Normalized binding density before and after EGF stimulation. Four distinct gene clusters shown in Figure 2 (clustering analysis) were used to plot the average profiles and heatmaps herein to show the binding signals before and after EGF stimulation. Top panel: average profiles of normalized protein bindings across genes in each cluster. The differential bindings of proteins compared to input control are shown in log₂(FC) scale. A positive number means an increase of chromatin binding compared to input control. Bottom panel: heatmaps of normalized binding of proteins across genes. The gene body with additional 5kb from TSS and TTS are shown in the x-axis. Concurrent recruitment of proteins in gene cluster 1 is specific to EGF treatment.

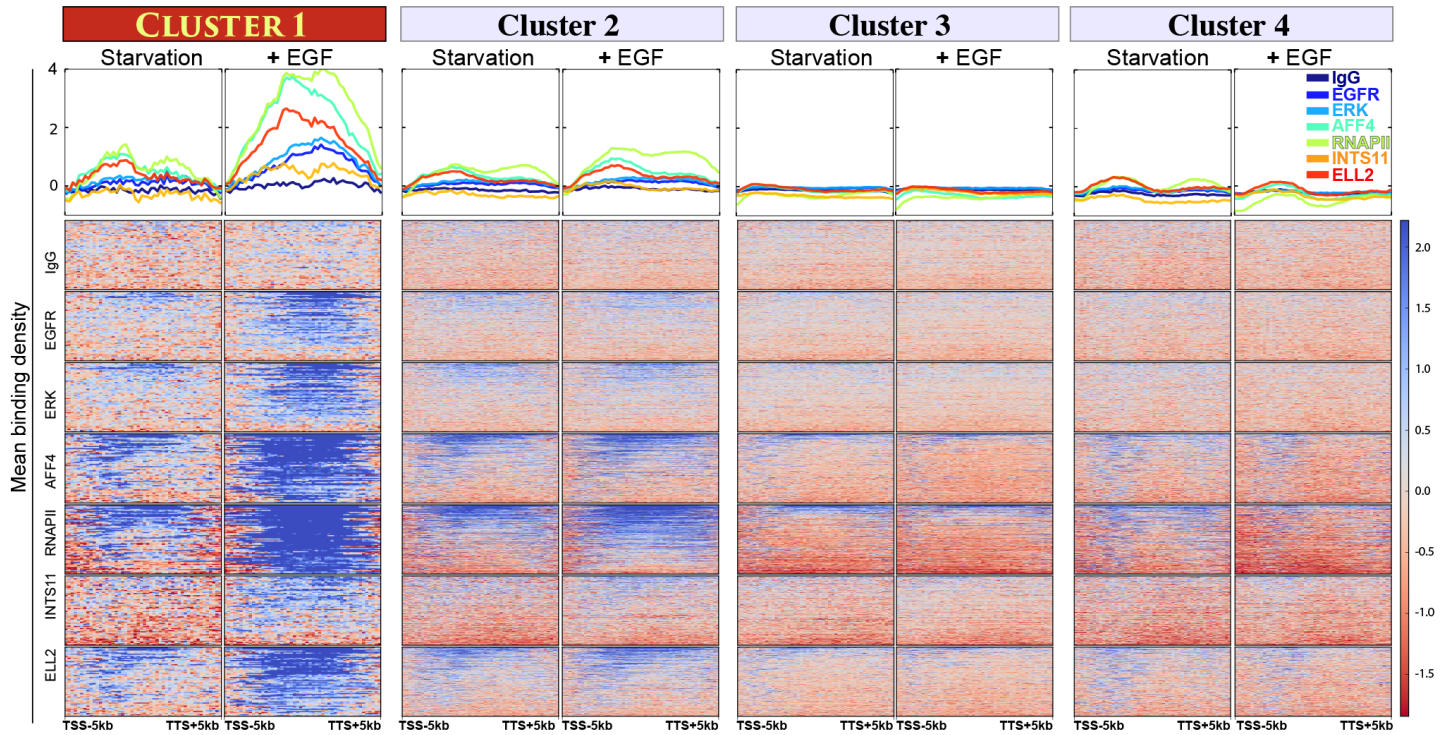
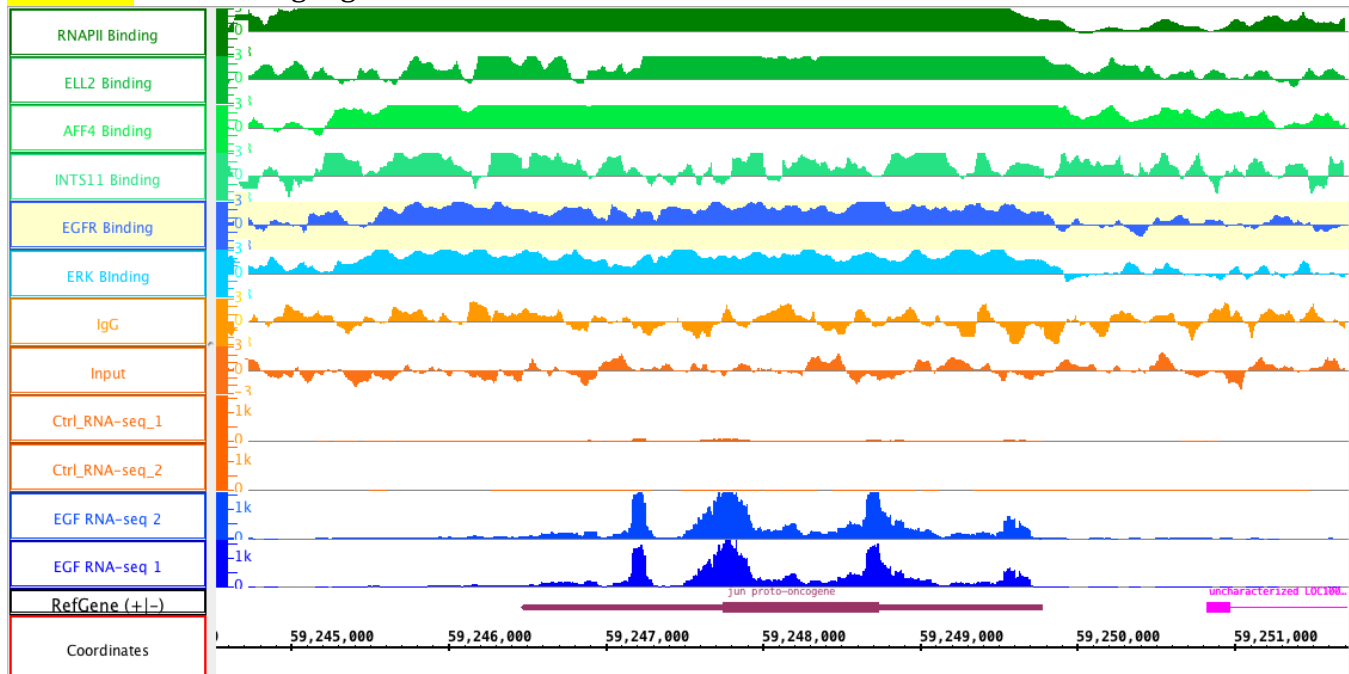


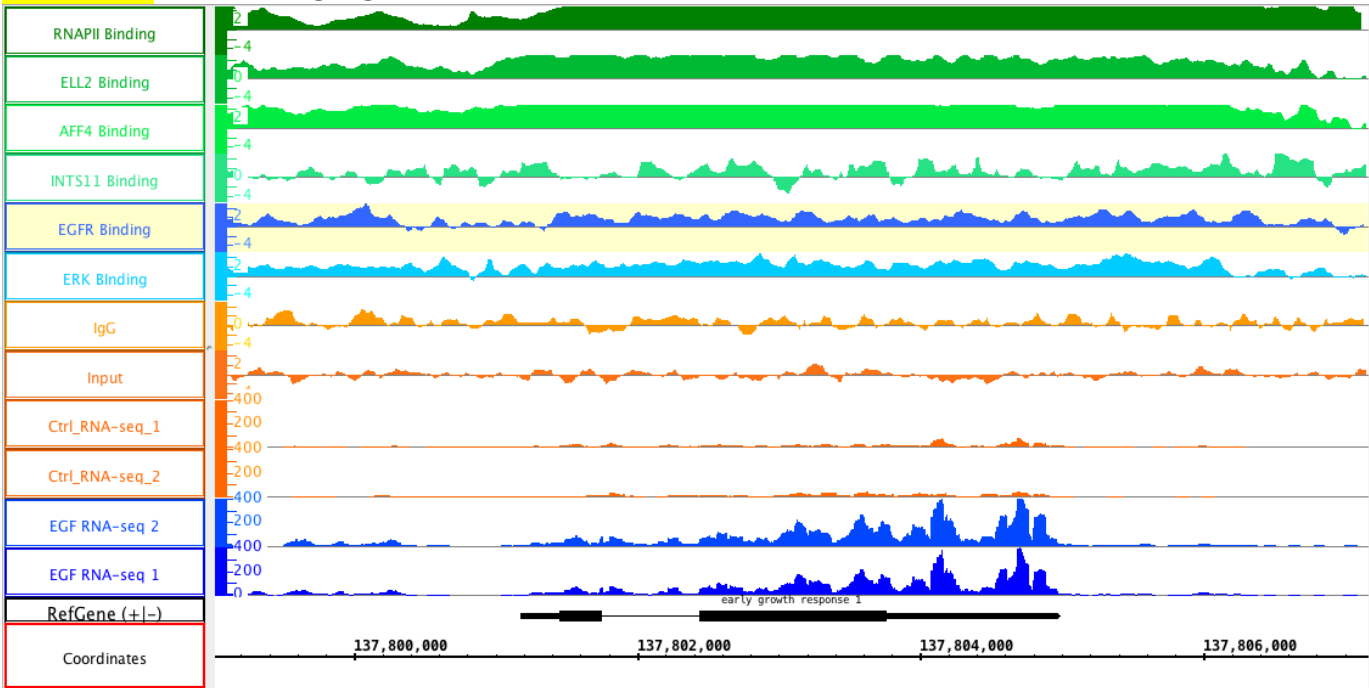
Figure S2:

Genome browser visualization of ChIP-seq and RNA-seq signals. Genes highlighted in yellow are the nEGFR target genes identified in the BETA analysis (i.e. *JUN*, *EGR1*, *FOS*, *IER2*, *DUSP1*, *DUSP2*, *DUSP5*, *FOSL1*, *JUNB*, *KLF2*, *CCNL1*, and *RHOB*). Genes highlighted in red indicate the genes with moderate recruitment of EGFR, as inspected in genome browser (i.e. *FOSB*, *N4A1*, *N4A3*, and *ZFP36*). Genes with no recruitment of EGFR are highlighted in green. They are negative control for comparison (i.e. *ZFP36L1*, *DUSP3*, and *DUSP8*). For each gene, the scales are the same for all the visualized ChIP-seq tracks and RNA-seq tracks.

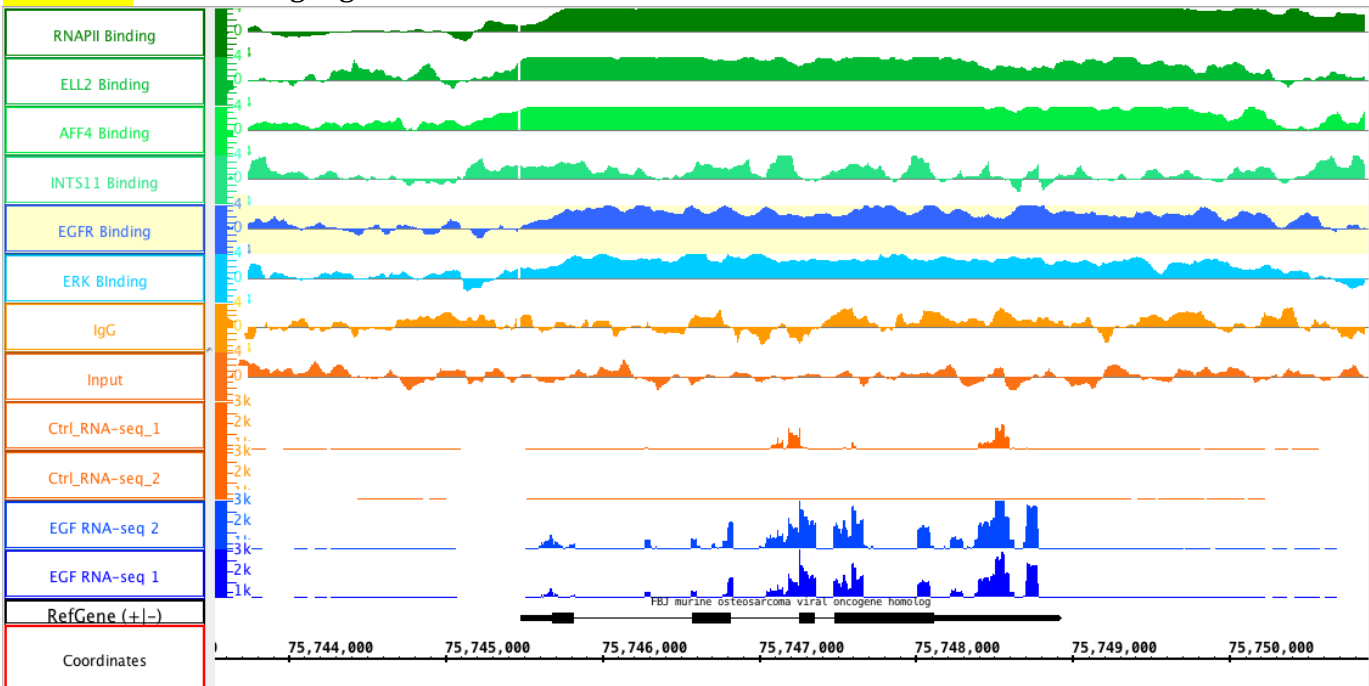
[JUN] - nEGFR target gene



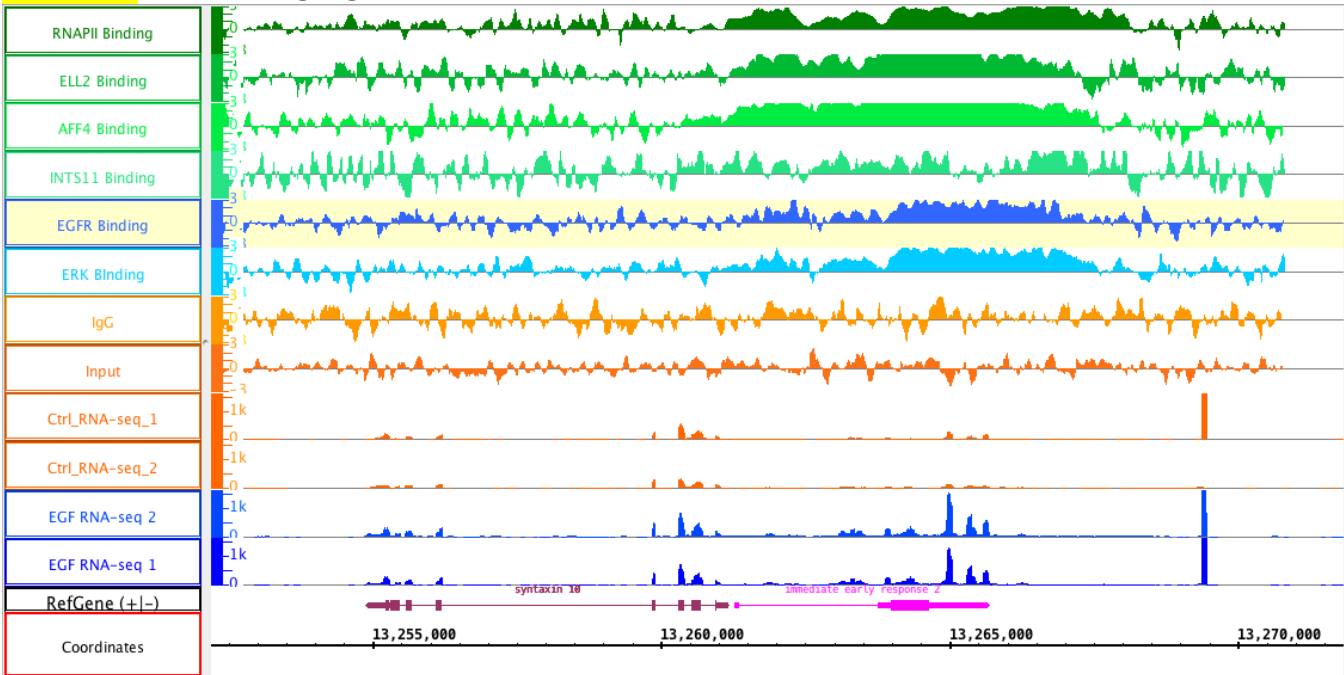
[EGR1] - nEGFR target gene



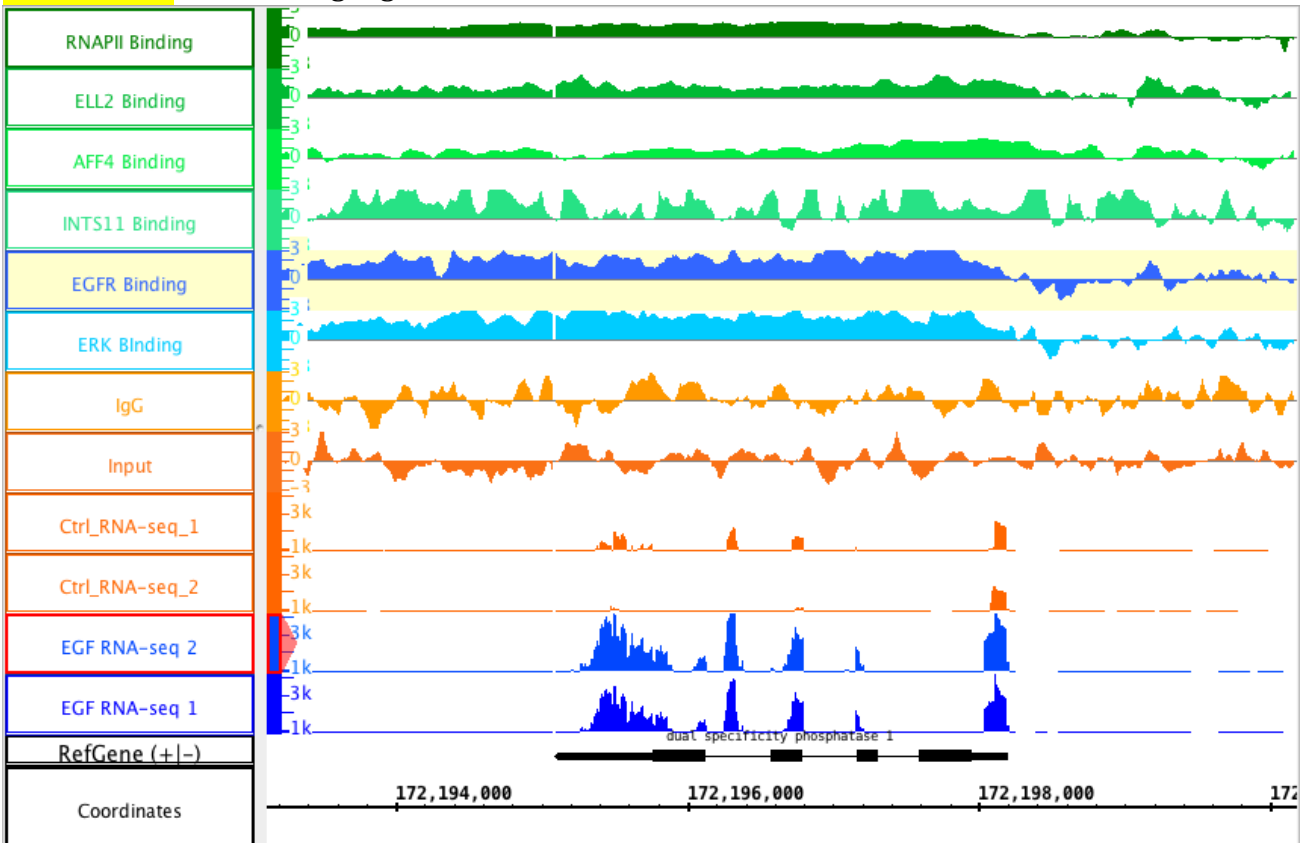
[FOS] - nEGFR target gene



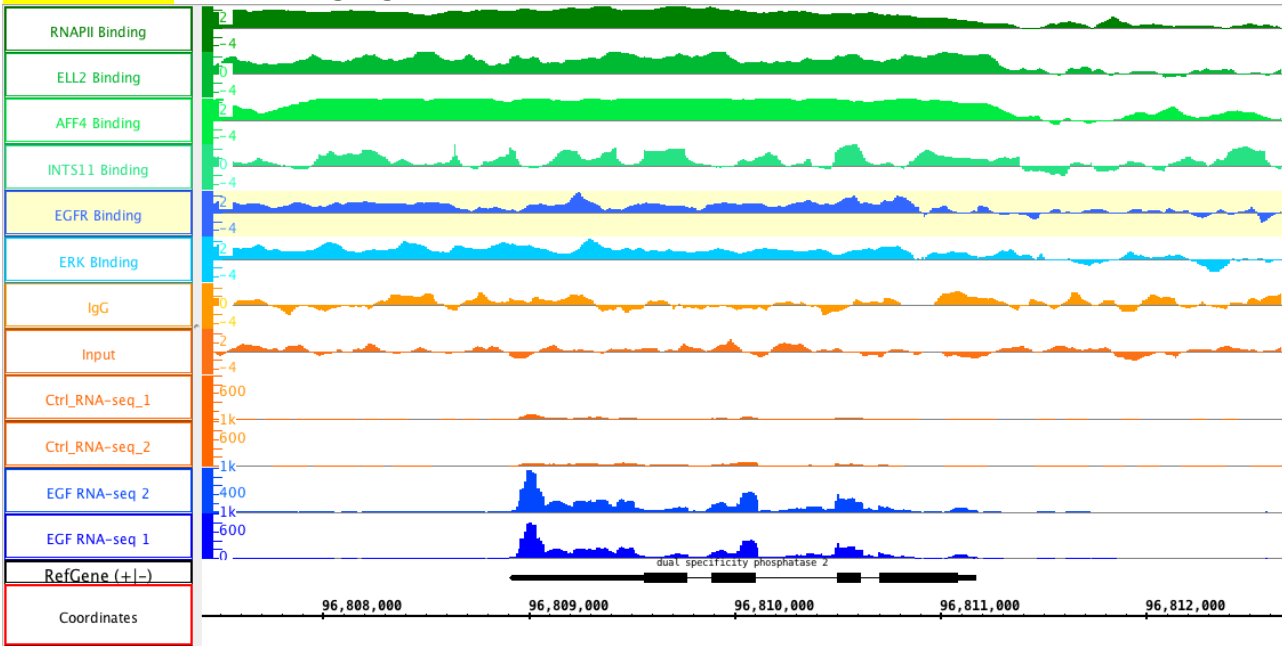
[IER2] - nEGFR target gene



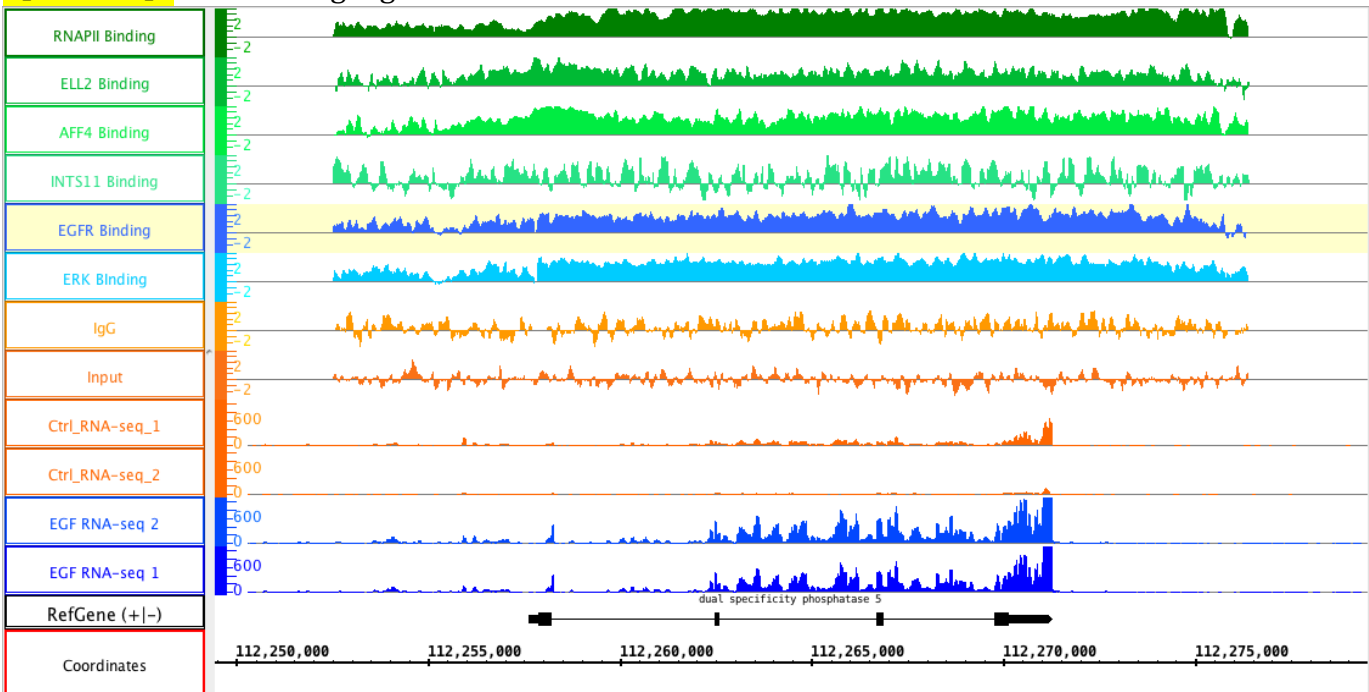
[DUSP1] - nEGFR target gene



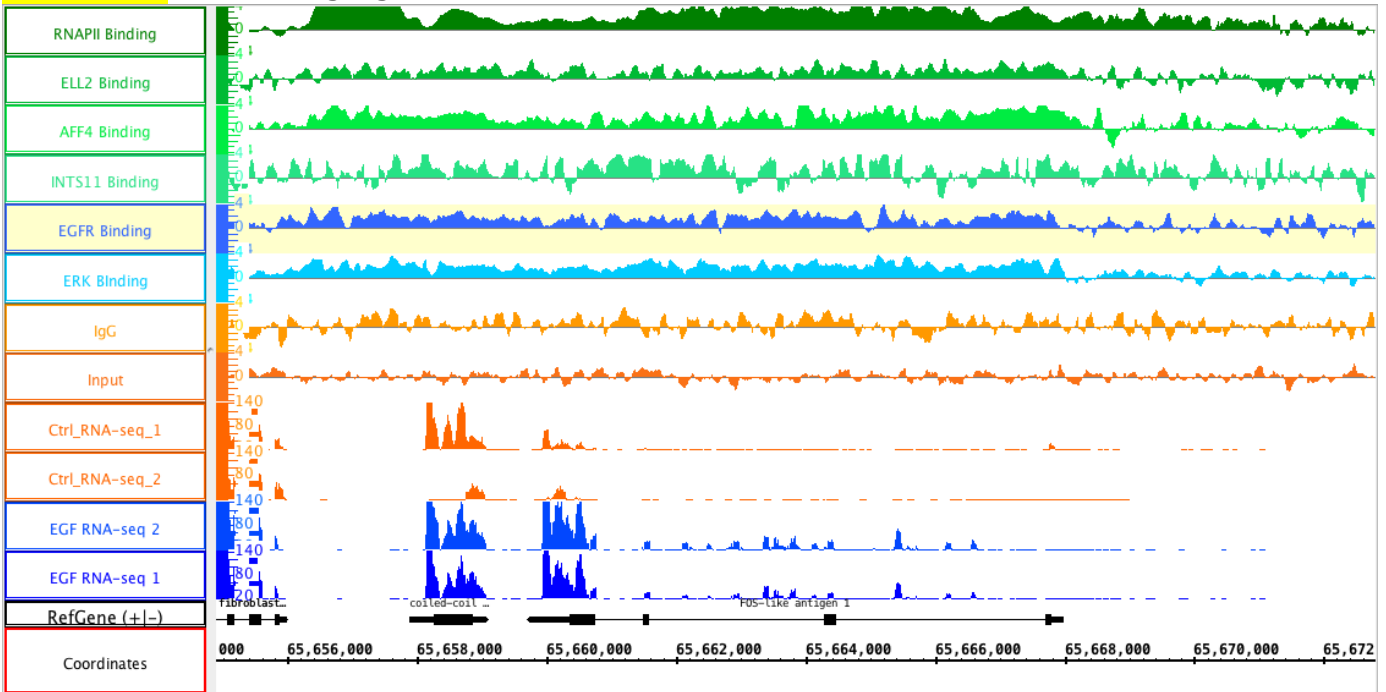
[DUSP2] - nEGFR target gene



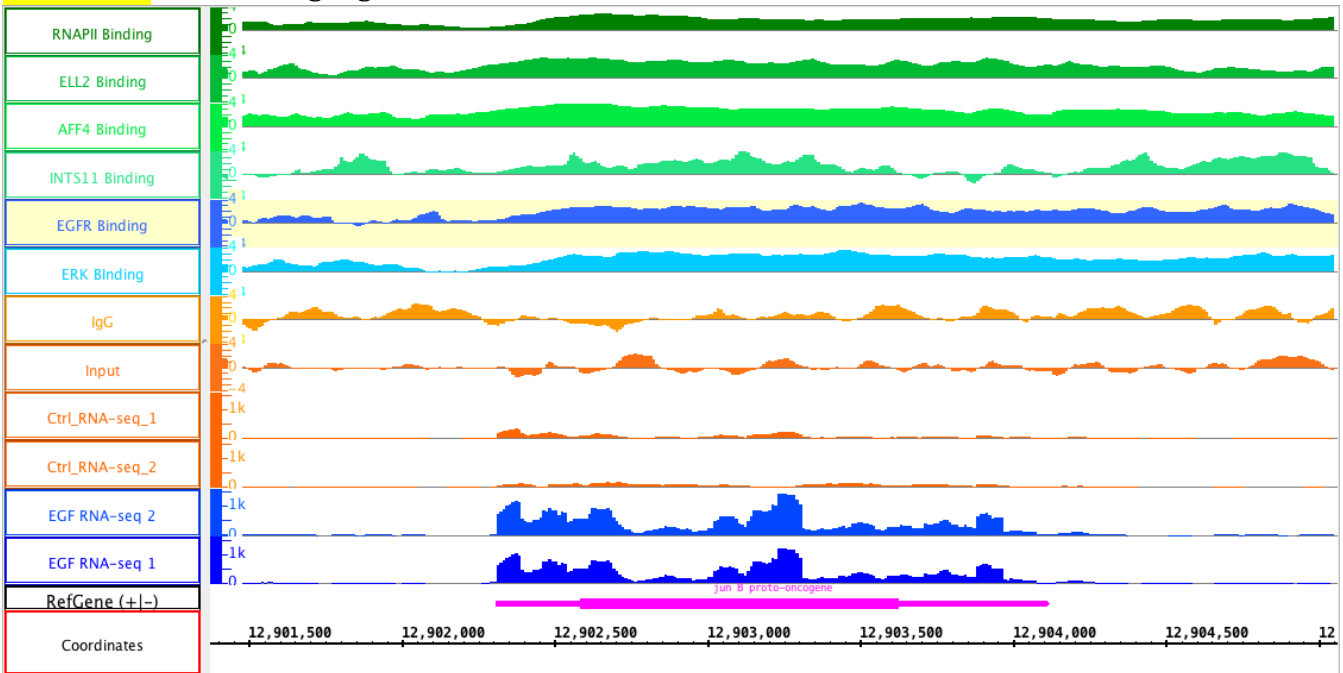
[DUSP5] - nEGFR target gene



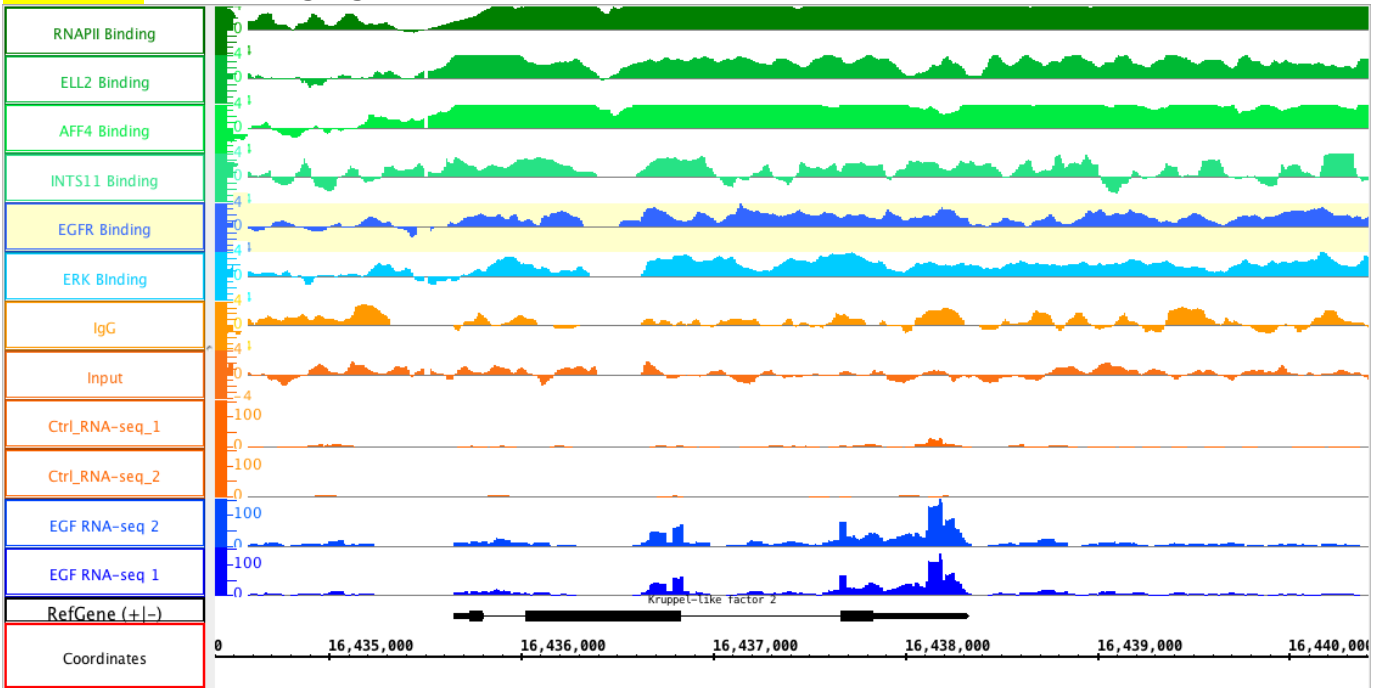
【FOSL1】 - nEGFR target gene



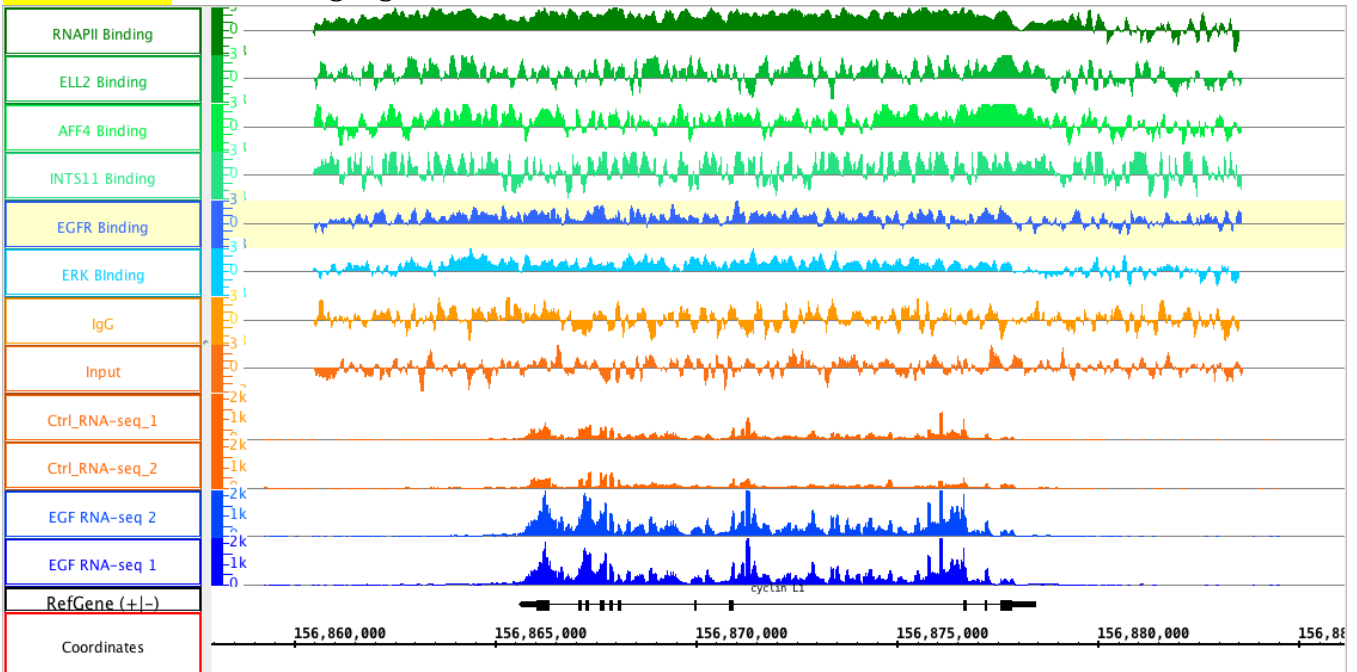
【JUNB】 - nEGFR target gene



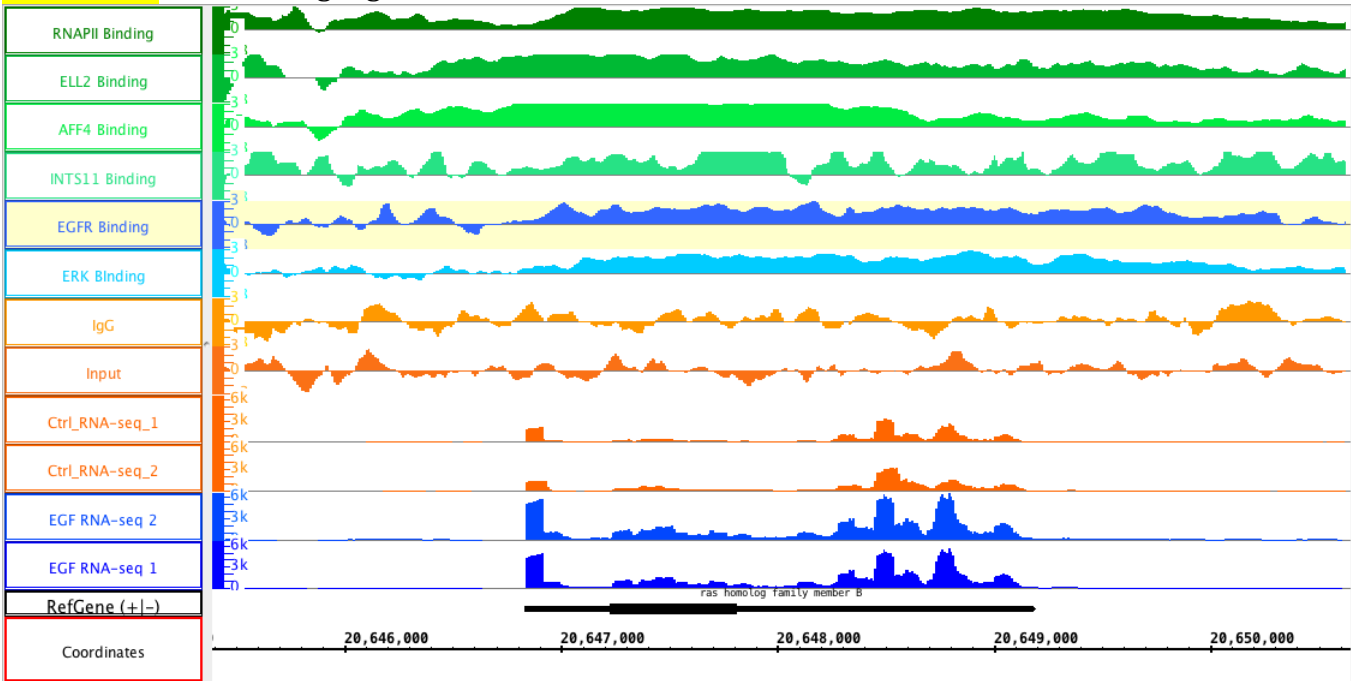
[KLF2] - nEGFR target gene



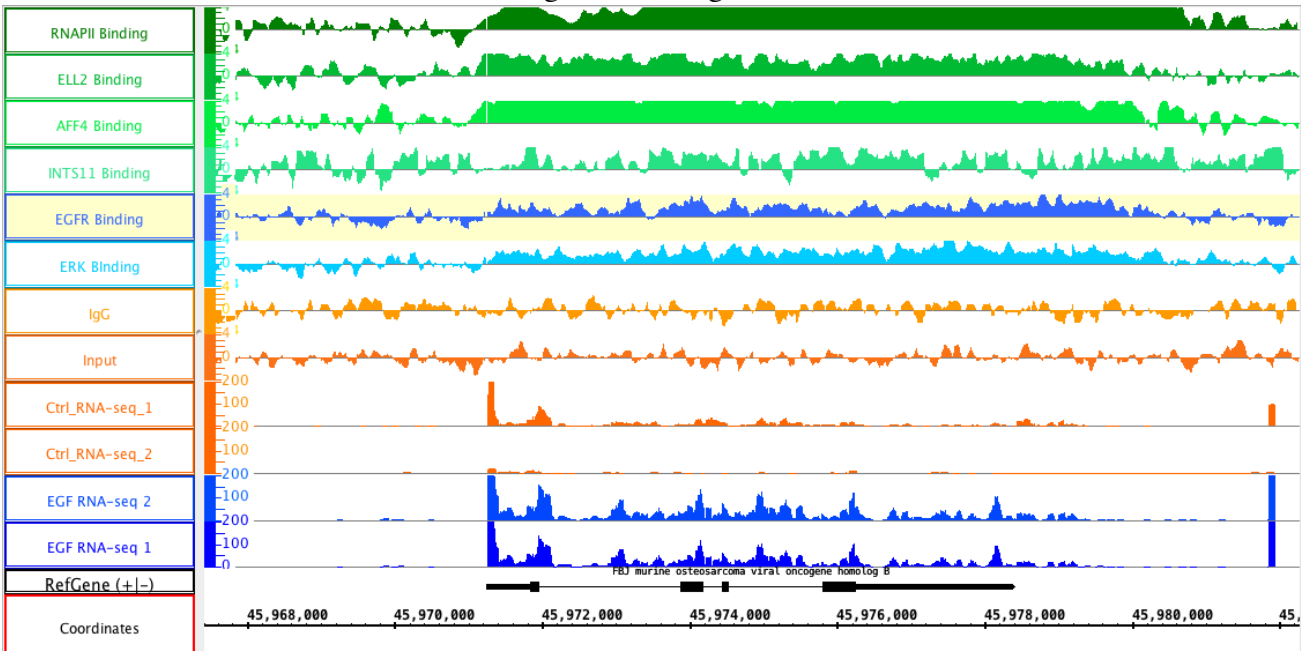
[CCNL1] - nEGFR target gene



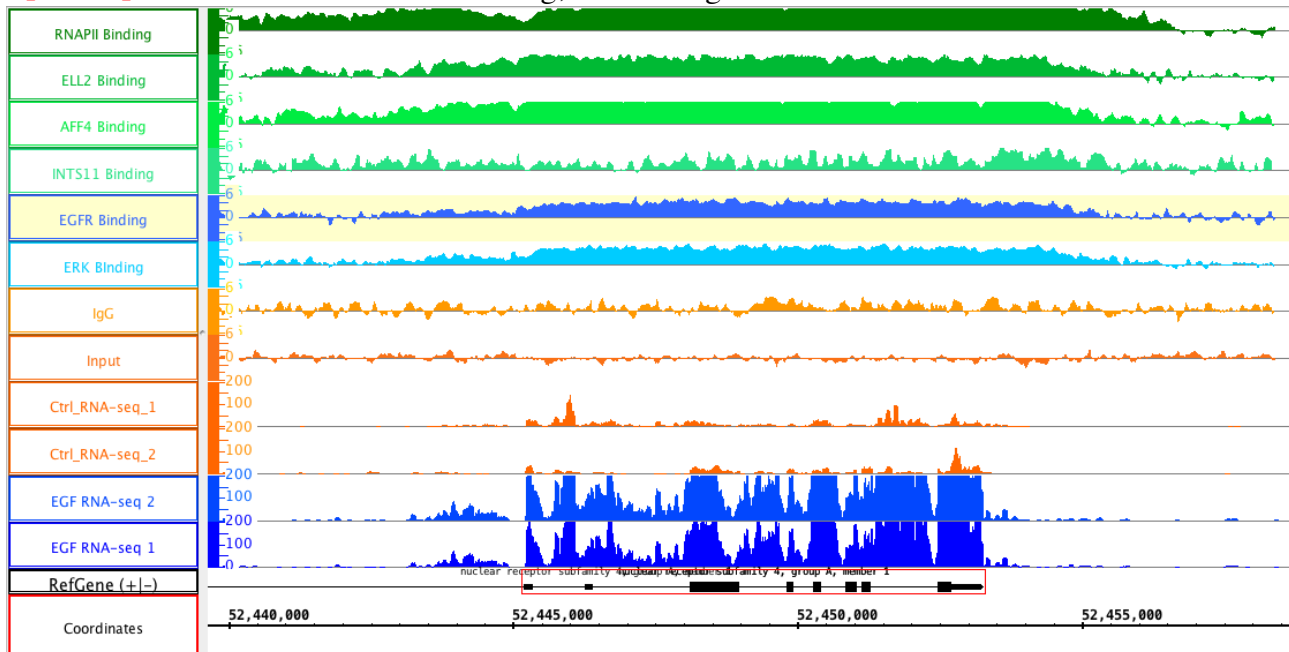
[RHOB] - nEGFR target gene



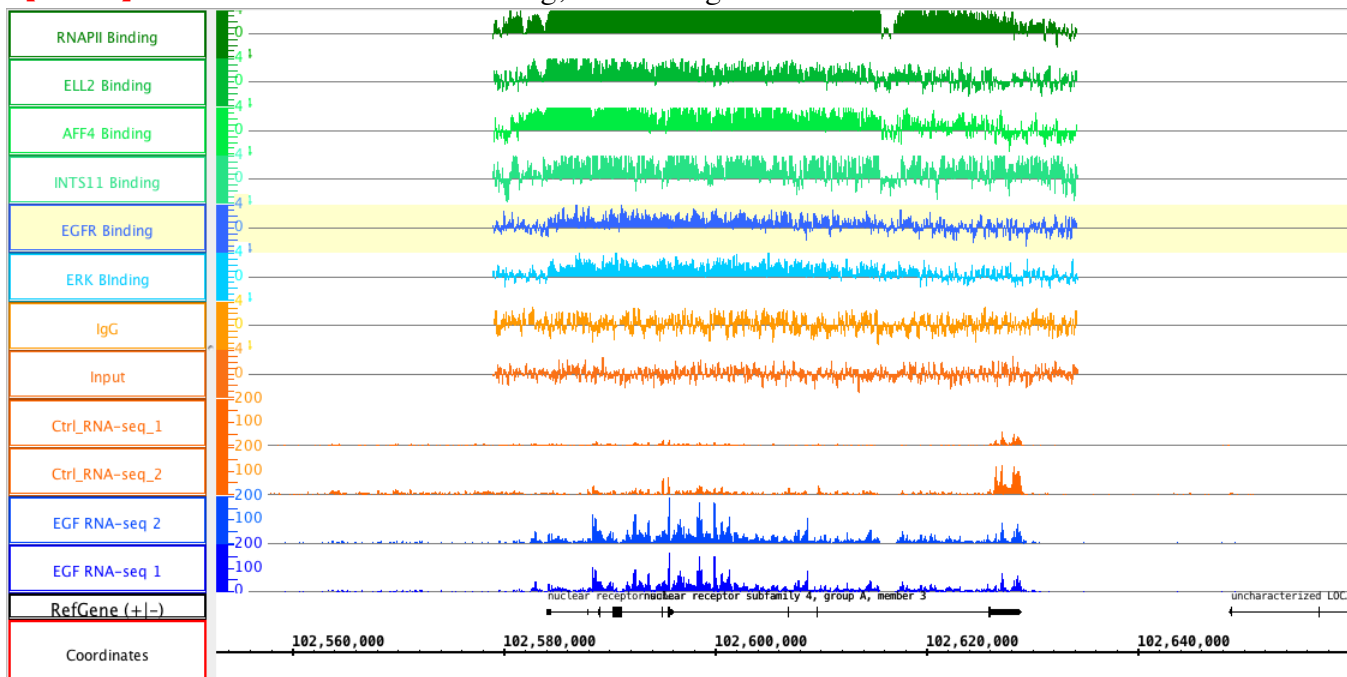
[FOSB] -with moderate nEGFR binding, as seen in genome browser



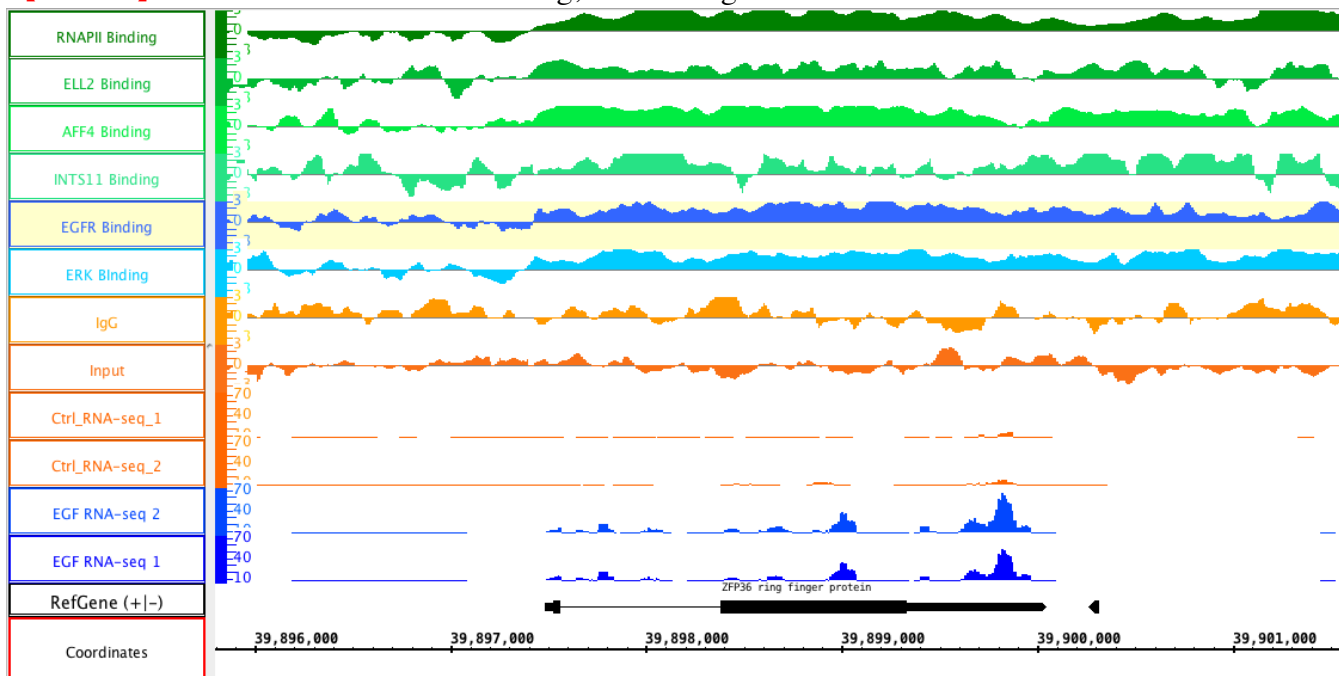
[N4A1] -with moderate nEGFR binding, as seen in genome browser



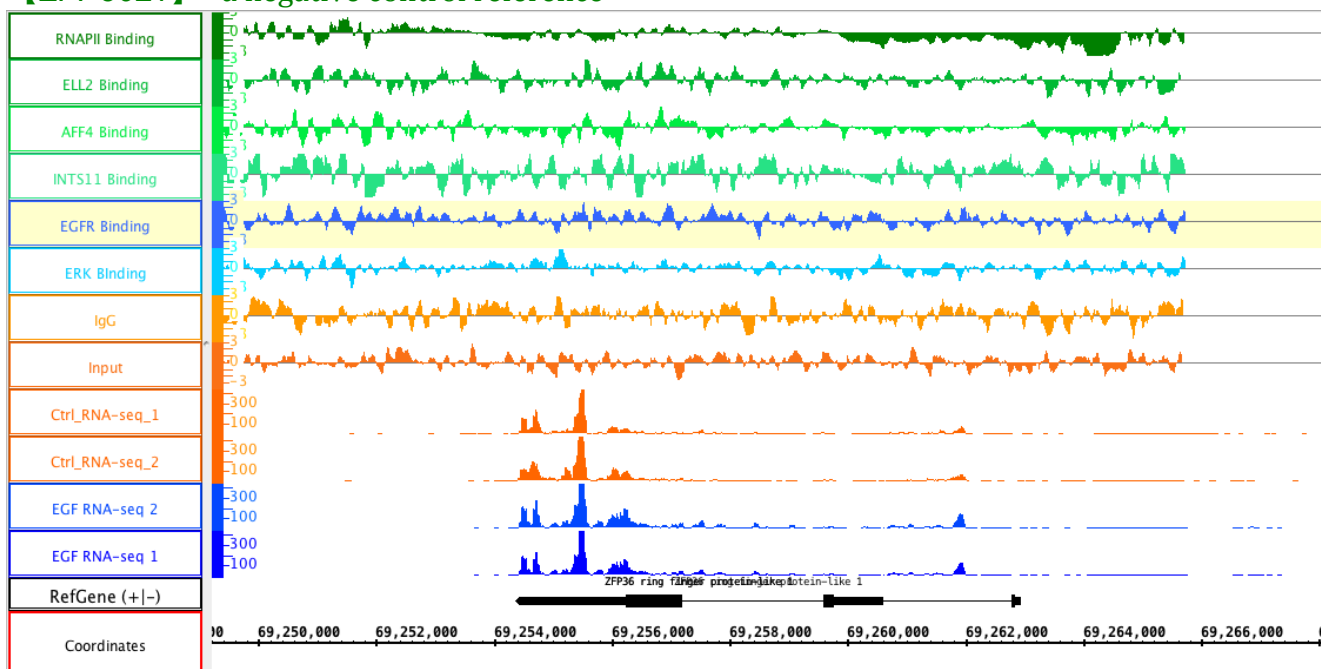
[N4A3] -with moderate nEGFR binding, as seen in genome browser



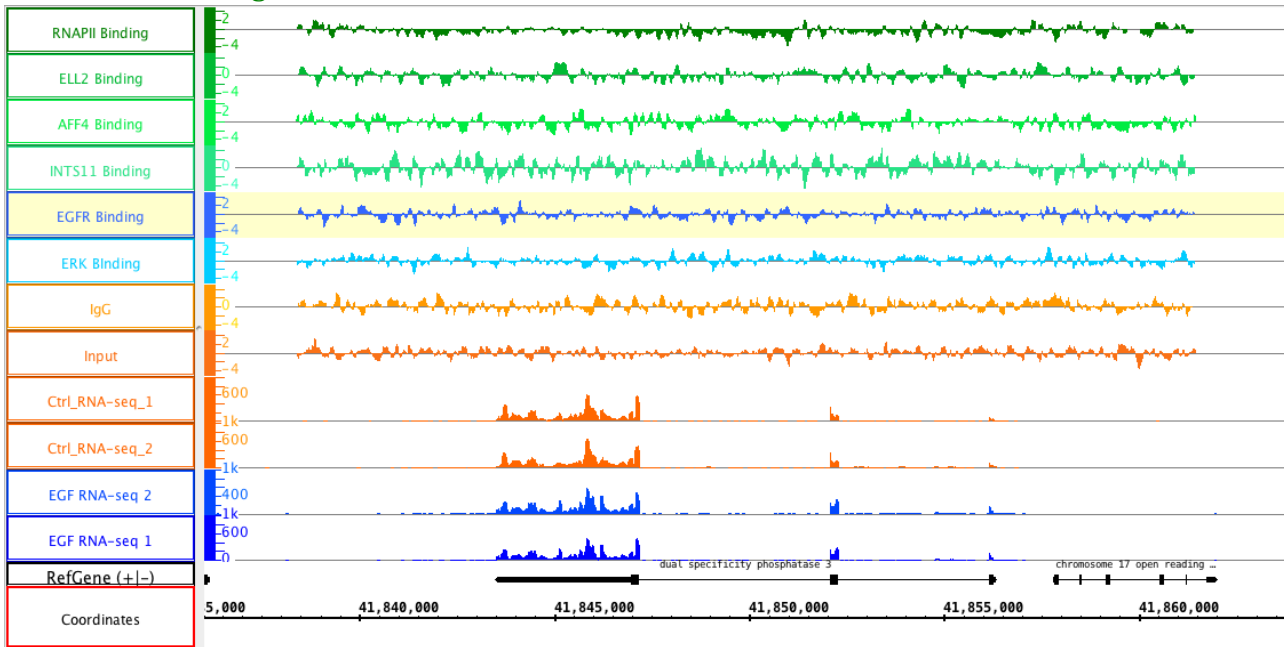
[ZFP36] -with moderate nEGFR binding, as seen in genome browser



[ZFP36L1] - a negative control reference



[DUSP3] - a negative control reference



[DUSP8] - a negative control reference

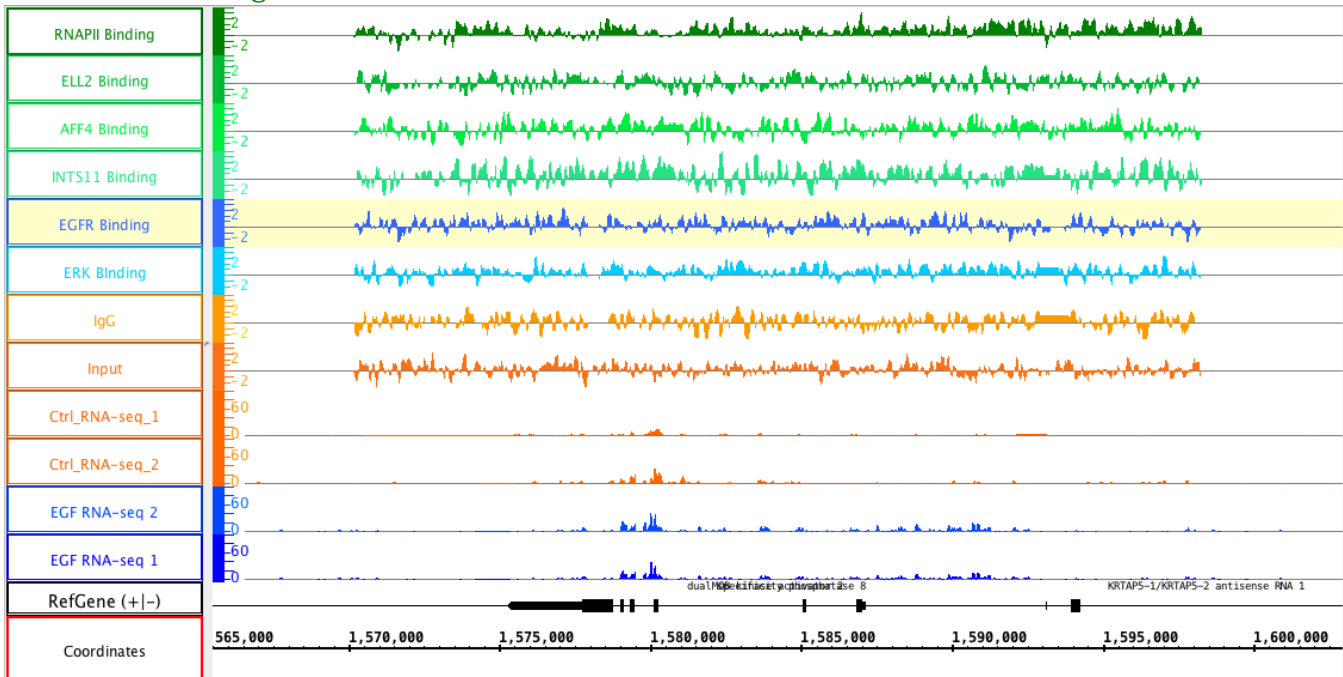


Table S1: ChIP-seq and RNA-seq data used in this study

GEO dataset	Name	Description
SRR1773226	pEGFR_control_repl_1	ChIP-seq of EGFR before EGF
SRR1773227	pEGFR_control_repl_2	ChIP-seq of EGFR before EGF
SRR1773228	pEGFR_EGF20_repl_1	ChIP-seq of EGFR after EGF
SRR1773229	pEGFR_EGF20_repl_2	ChIP-seq of EGFR after EGF
SRR1773230	pERK_control_repl_1	ChIP-seq of ERK before EGF
SRR1773231	pERK_control_repl_2	ChIP-seq of ERK before EGF
SRR1773232	pERK_EGF20_repl_1	ChIP-seq of ERK after EGF
SRR1773233	pERK_EGF20_repl_2	ChIP-seq of ERK after EGF
SRR1342254	RNAPII_0min_rep1	ChIP-seq of RNAPII before EGF
SRR1342256	RNAPII_0min_rep2	ChIP-seq of RNAPII before EGF
SRR1342255	RNAPII_20min_rep1	ChIP-seq of RNAPII before EGF
SRR1342257	RNAPII_20min_rep2	ChIP-seq of RNAPII before EGF
SRR1342222	AFF4_CTRL_rep1	ChIP-seq of AFF4 before EGF
SRR1342226	AFF4_CTRL_rep2	ChIP-seq of AFF4 before EGF
SRR1342223	AFF4_CTRL_EGF_rep1	ChIP-seq of AFF4 after EGF
SRR1342227	AFF4_CTRL_EGF_rep2	ChIP-seq of AFF4 after EGF
SRR1342230	ELL2_CTRL_rep1	ChIP-seq of ELL2 before EGF
SRR1342234	ELL2_CTRL_rep2	ChIP-seq of ELL2 before EGF
SRR1342231	ELL2_CTRL_EGF_rep1	ChIP-seq of ELL2 after EGF
SRR1342235	ELL2_CTRL_EGF_rep2	ChIP-seq of ELL2 after EGF
SRR1342246	INTS11_0min_rep1	ChIP-seq of INTS11 before EGF
SRR1342248	INTS11_0min_rep2	ChIP-seq of INTS11 before EGF
SRR1342247	INTS11_20min_rep1	ChIP-seq of INTS11 after EGF
SRR1342249	INTS11_20min_rep2	ChIP-seq of INTS11 after EGF
SRR4015769	CTRL (Input)	ChIP-seq input control before EGF
SRR4015770	EGF20 (Input)	ChIP-seq input control after EGF
SRR1773234	IgG_control	ChIP-seq of IgG control before EGF
SRR1773235	IgG_EGF20	ChIP-seq of IgG control after EGF
SRR1342238	CTRL_RNA_rep1	RNA-seq before EGF
SRR1342242	CTRL_RNA_rep2	RNA-seq before EGF
SRR1342239	CTRL_EGF_RNA_rep1	RNA-seq after EGF
SRR1342243	CTRL_EGF_RNA_rep2	RNA-seq after EGF

Table S2:

TCGA data used in Kaplan-Meier Analysis and Cox proportional hazards analyses

TCGA provisional data set	Patient Number with available OS* data
Bladder Urothelial Carcinoma	405
Brain Lower Grade Glioma	516
Breast Invasive Carcinoma	1090
Cervical Squamous Cell Carcinoma and Endocervical Adenocarcinoma	302
Colorectal Adenocarcinoma	371
Esophageal Carcinoma	184
Head and Neck Squamous Cell Carcinoma	518
Kidney Renal Clear Cell Carcinoma	530
Lung Adenocarcinoma	504
Lung Squamous Cell Carcinoma	493
Ovarian Serous Cystadenocarcinoma	250
Pancreatic Adenocarcinoma	178
Prostate Adenocarcinoma	496
Sarcoma	258
Stomach Adenocarcinoma	404
Thyroid Carcinoma	500
Uterine Corpus Endometrial Carcinoma	175

* OS = Overall Survival

Table S3:

The genes in the cluster 1 identified by K-means unsupervised clustering analysis

Gene Symbol	Gene Symbol
BTG2	ACTB
FOS	ACTG1
JUN	ARC
ZC3H12A	C19orf71
ATF3	CCDC64B
CCNL1	CCDC85B
DUSP2	CFL1
DUSP5	COL7A1
EGR1	CSRNP1
EGR3	CSRP1
IER2	DNAJB1
JUNB	EGR2
KLF2	EPPK1
KLF6	ETF1
NR4A1	EZR
ZFP36	FASN
CTGF	FLNA
CYR61	FZR1
FOSB	HMG20B
LDLR	HSPA8
NR4A2	IDI1
NR4A3	MFSD12
RHOB	MT1E
FOSL1	SNORA31
JUND	SOWAHC
MAFF	THOC6
MCL1	WDR1
THBS1	
TM4SF1	
TPM4	
KRT17	
MT1X	
MT2A	
ZYX	

Table S4: Gene ontology (GO) analysis of EGF-responsive gene cluster 1.

GO	Biological Process	Adjusted P-value	Z-score	Combined Score
1	Positive regulation of transcription initiation from RNA polymerase II promoter	1.38793E-08	-6.55	158.09
2	Positive regulation of transcription from RNA polymerase II promoter involved in neuron differentiation	1.38793E-08	-6.74	156.57
3	Positive regulation of purine nucleotide biosynthetic process by positive regulation of transcription from RNA polymerase II promoter	1.38793E-08	-6.49	142.43
4	Positive regulation of ribosomal protein gene transcription from RNA polymerase II promoter	1.38793E-08	-6.48	142.22
5	Positive regulation of peroxisome organization by positive regulation of transcription from RNA polymerase II promoter	1.38793E-08	-6.48	142.12
6	Regulation of glycolytic process by positive regulation of transcription from RNA polymerase II promoter	1.38793E-08	-6.48	142.12
7	Regulation of cellular ketone metabolic process by positive regulation of transcription from RNA polymerase II promoter	1.38793E-08	-6.48	142.10
8	Positive regulation of termination of RNA polymerase II transcription	1.38793E-08	-6.47	141.90
9	Positive regulation of filamentous growth of a population of unicellular organisms in response to starvation by positive regulation of transcription from RNA polymerase II promoter	1.38793E-08	-6.47	141.88
10	Positive regulation of SREBP signaling pathway	1.38793E-08	-6.50	141.83

Table S5: Activating/ repressive function prediction

ChIP Target	<i>p</i> value for activating function	<i>p</i> value for repressive function
EGFR	5.55E-05	0.981
ELL2	3.09E-11	0.422
INTS11	1.05E-09	0.052
RNAPII	1.30E-05	0.00573
ERK	1.30E-05	0.768
AFF4	5.55E-05	0.0275
IgG-1	0.449	0.535
IgG-2	0.638	0.768

Table S6:

Up-regulated genes targeted by chromatin-bound nEGFR.

Yellow highlighted genes are genes presented in EGF-responsive gene cluster 1

Chroms	RefseqID	Rank product	Strands	GeneSymbol
chr2	NM_004418	1.48E-07	-	DUSP2
chr19	NM_016270	1.60E-07	+	KLF2
chr5	NM_001964	2.50E-07	+	EGR1
chr2	NM_004040	2.57E-07	+	RHOB
chr10	NM_004419	2.69E-07	+	DUSP5
chr5	NM_004417	2.82E-07	-	DUSP1
chr1	NM_002228	4.62E-07	-	JUN
chr14	NM_005252	4.75E-07	+	FOS
chr19	NM_004907	5.07E-07	+	IER2
chr19	NM_002229	6.86E-07	+	JUNB
chr11	NM_001300855	7.70E-07	-	FOSL1
chr3	NM_020307	1.57E-05	-	CCNL1

Table S7:

ATRS sites (in red; either TNTTT or TTTNT; N is any nucleotide) on the promoters (1500 upstream from TSS) of nEGFR target genes. Green indicates the flanking sequences around ATRS sites in various lengths.

<p>JUNB (10 ATRS sites)</p> <p>GACAGGGCCGGGCTCCTTCCCCGGGGCTGTTGCCACACTTCTGCCTCTGCGCTCTTTCC CCCAGCCTGTTTCTAAGGAAGGGAGTGGGGTTGGCGACC GCCGCCAGCCGTGGGGCTC TCTCCTTACCCGGGCTAGCAGATGACCCCAAGTGGTCCCCAATTTCTGGCAGACATGTCT CCATCTTCTACCTGGCATATTTACCTGCCTCAGTGTACCCAGGCCGCTTACTAGCTTT GACTCAGCTCCCATGAGCTCCTGGACCCCTACTCATTTCTTGCAATTTAATGGGTCATGC TCCCATTACAGTGTCTAACCCCATTTCTGCTTTTGGGGTCTCCCAATGGATTGTCA GTCCCTCCTACCCCTCTCGTATTCTGGGTACCTCAGGGGTTTCTTGACACATACTGGGACC CTCACCCCACTGCTGCGTACCAGGTCTGGTATTTGTCCCACTGGACTCCAGGAAATC CCGCTGTTTACAAGGACACGGCTTCTGACAGTGACGCGAGCCGCTCCTCCCTTCC</p>
<p>RHOB (7 ATRS sites)</p> <p>TCCTGCTTGTGTTCAAGGTGTTTCTCCTGCCCGGGAGCCCTCCCGACTCCCTTTCCCC CTATCCCTTCTTCCTCTTTTATCCGTAGAAATCGGTTGACTTGGGTCTTTCCGGATCAC CATTCTATTGTACAATAGTGTATATTCTATTGTACATTTATCTCAGACAGTCTCTGT AAAAGAAAAGAGAAAACACTCTGTTTGGGAACAAAAGTGTGTGTGGGGTGTGTGTGT GTGTGTGTGTGTGTGTGTTGTTTATTTAAAAACAAAACCAAGTAAAAGAGCTGCC CGGCTATATTAAGAAAGTGGCCGACTTCTTTAAATAGCGGGCGCTAGGGCCGACGCCCT</p>
<p>CNL1 (12 ATRS sites)</p> <p>ACAAAAATGGAAGAAAACAGAAAACGGTGTCAATTTTGTTTAAGGAAACCGAGGC TCCTTTAAAAGTTTGTTATAAAATATAGATATCTATAAAATTTAGAGTGGAAAGATT TTTATCTTTTTTTCATAGGGGAAAGGGTAGATGAGAAATGTAGACATTTATTTTGAG GAGCAGCAAAATGATTATTAGGAACAATGAATGGACAGAAATAGTAAATATTTCTTT GAGTAATCTTGTGAAAAAGTCCCTCCAGGAATGGCTGCATTTCTGAGTCTTTTTGAAATA GTCAAGTGTGGGGACCTGCATTATGAGGCAGCTTCTAAAGCCTCTTCTTTGGGGTATC GCTTTCTGAGCGTCAAGAGTAAAACGTGATGCATTCCTTCTTCCCAACCTAGATTCTAG TAGTTTAGATCAGTATCATTGTTTTACTTCAAGGTTCAAGAAACGCTGGAAATGTCTAG CTAAGACTATTTTTGGAAACTAGGGATTTTCCAGATTACTGAAAGCCGTGGCGGTGCA</p>
<p>EGR1 (4 ATRS sites)</p> <p>CCCCTCTTTCGGATTCGCCAGTGTGGGCCGGCCCTCCACCTGGACTGGATAAAGGGGGG TTGGGGCAATCAGCTTCCCACTTCGGTCCCCAAAGGTGGGGTCTTTCCGGCCGGGGAC GAGCAGGAAGGATCCCCCGCCGGAACAACCCTATTTGGGCAGCACCTTATTTGGAGTGG</p>
<p>KLF2 (8 ATRS sites)</p> <p>TGACTGTATCACCGTCTCTGAGTTACTTAATTCATTTTATGGAAAGTCAAGTAAAGGAAC TTAATGTGTCTTGTGTTTACCACACAAAAGTTTTGTTTTGTTTTTTGGAGACAGT TCCTGGGCTCAAGCGATCCTCCACCTCAGCCTCCCACTACACCCAGCTAATTTTTTTA TTTTTTAAGAGATGGGGCCACTGTGTTGCCAGGCTGGTCTTGAACCTCGCCCTCGAG GCTTACACAAGGTGTTTTTTTTACAGGGTGTGTGCACACGGTGGGTCCCTCTGGGTGG</p>
<p>FOS (5 ATRS sites)</p> <p>ACACCCCTTCAAATGTCTTCCACAGTGGTTTGCACAGTGTTTATCTGCTGGTGTCTC CGCGTGTCTTCTTTAAAAAAATAAATAAATAAGTACCCAGTATCGTAAAGTAGGTTATC GTATTCTCTTATTTTGGATCCTCCACTTTTCTGCTTCCAAACCGCAGGAACAGTGTAGTAT TCCTCGGGTCTGTACTCGATGCCGTTTCTCCTATCTGTGAGCCTCAGAACTGTCTTCA</p>
<p>DUSP2 (4 ATRS sites)</p> <p>TTCAAGACGGTCTGGACACAGGGGTCTGTGGGGGAGCCGGAAGGGTCTTTCAGAGGGCAC TCACCCGTGGCAGCAGGCATTTGTCATGTTTGTGGTGACAAATTTCTAAGAGGAAAAAT</p>
<p>IER2 (1 ATRS sites)</p> <p>ATCCGCTCCAGGAACACCTTTCTCTCCTGCAGGTCCCGGCTGGGAGCTTGAACCTGCCT</p>
<p>DUSP5 (5 ATRS sites)</p> <p>GCGGGCAGACTTGTTTCCATCAAGCAGTCCCAGCCAGGCTAACAAATAAATGGTTGGCAG TGAGCTTGGGGCAGAAACTGTTTCCATCCATGTGTCCCGCAGCTAGCAAAAGCCCTGG CACCGCCGACCCCAACCCCGTTTTTACTTTTACAAACTTTATTATGAAAAATATCAA GCCCGCCCTGCAGGGCTGGCCAGGGCCGAGGGGGGGGAAACCCCATATTTGGC</p>
<p>FOSL1 (12 ATRS sites)</p> <p>CTCTTGATCTATTTACTTTGAGTCTTGTCTGTCCCCAGGCTGGACTGCAGTGGCGCAG GAACAGCTGGGACCAAGGCAGGCTACCACCATGTCCAGAAAATTTATAATTTTTTTG TAGAGATGGGGTCTCAAATGGTTCTTTCTGCCCTTGGCCTTCCAAGTGCTAGGATTACAA GCATGAGCCACACCTGGCCCCAGCCTCTTTCTGTAGTCTGTGACAACCTGACAGCT TGGCGTTTATCAGACCTCAGGACACCTGTAGTGGCCCTGAATAAAACCTCGTTATAGCTC CTGAAATTAATCCTGAGTAATACTATTATTTGCATTTTATTGGGGTTAGTTCAAAGCAT GTAAAAATAAATATGCCACCATTTTTGTAAACCTGGTTTGTCATTTATCACTTTTTCATA GGTTGGCGTGGCTCCTAGAGATGTATTCTTTCGTGCTTATTTTGTGGGAGCAGAAACGGGA</p>
<p>JUN (4 ATRS sites)</p> <p>TGCGAGGATGGAACCTGCGAGGCGAGGGGAGGGGAGCGGGTGTTTGGCCACCACCTCCCT ACTGTGTAGCCTGGCCACGAAAGAACCAGGATTCCCGACTTCGGGATTCTTTCCACCAC TTTATCGGAGTGTCCGCGCCCTTCTGGGCTTGTTTTCCCGAAAGCAACTCGGCGGGATG</p>
<p>DUSP1 (9 ATRS sites)</p> <p>TTTTCTAGAAGAATCCAGGCAGAACATTTGCGCAGGCGAAAAACACAAAGCTAAGCGAGG GGGTGGCGCAATGTTTATGTTTGTGTACCCAGCGCTCGCGTCTGCTGAGCAGGCTCCGC GGGTTGGAGGCCCCAGCCAGCGCTTGTGGGCGCTCACTGTGTATACTCTTTGT TGCCCTCCCTGGCTCCAAGTCTTCCGGGGGCCAAAGACTAGGAATAGCATTATTTCCCCG GTGGGAGTTTGTCTGCACACTTTCATGGCAAAATGAGATTATTTTAAGCCACCTTAAA CGGTCTTGGTAGGGACGACTTTTCTATCGGCAGAGTTGTTCATTTTTCTCTAAAACCTCAT CTTAGGCGCCTATTTGTGCCCCACCCAGTAGTGTGGTTCTGGGCAAGTCAGTCCGCT</p>

Table S8:

Transcription-related proteins identified in immune-precipitation assay followed by shotgun mass spectrometry analysis (data adapted from Mikula et al., 2016)

Name	IgG	Pol2-CTD	EGFR	MEK1/2	ERK1/2
DNA-directed RNA polymerase II subunit RPB1	0	28	9	0	0
Core histone macro-H2A.1	0	0	4	0	0
DNA replication licensing factor MCM2	0	4	0	0	0
DNA replication licensing factor MCM4	0	27	0	0	0
DNA replication licensing factor MCM6	0	15	0	0	0
DNA replication licensing factor MCM7	0	14	0	0	0
DNA topoisomerase 1	0	0	2	0	0
DNA topoisomerase 2-alpha	0	0	2	0	0
DNA-directed RNA polymerase II subunit RPB2	0	4	5	0	0
DNA-directed RNA polymerase II subunit RPB3	0	3	3	0	0
DNA-directed RNA polymerases I, II, and III subunit RPABC1	0	0	2	0	0
Histone H1.2	0	4	0	0	2
Histone H1.3	0	4	0	0	2
Histone H1.4	0	6	0	0	3
Histone H1.5	0	3	0	0	0
Histone H2A type 1	0	5	4	0	2
Histone H2A type 1-A	0	4	2	0	0
Histone H2A type 1-B/E	0	4	4	0	0
Histone H2A type 1-C	0	5	4	0	2
Histone H2A type 1-D	0	4	4	0	0
Histone H2A type 1-H	0	5	4	0	2
Histone H2A type 1-J	0	5	4	0	2
Histone H2A type 2-A	0	5	4	0	2
Histone H2A type 2-C	0	5	4	0	2
Histone H2A type 3	0	4	4	0	0
Histone H2A.J	0	5	4	0	2
Histone H2A.V	0	3	3	0	0
Histone H2A.Z	0	3	3	0	0
Histone H2B type 1-A	0	2	2	0	3
Histone H2B type F-S	0	5	4	2	5
Histone H3.1t	0	0	3	0	0
Histone H3.2	0	0	4	0	0
Histone H3.3	0	0	4	0	0
Histone H3.3C	0	0	2	0	0
Histone H4	2	6	7	3	3
Putative histone H2B type 2-C	0	3	3	0	0
Putative histone H2B type 2-D	0	3	3	0	0

Note: Numbers in columns are peptides detected from mass spectrometry analysis