SUPPLEMENTARY INFORMATION

Integrative Genomics of Gene and Metabolic Regulation by Estrogen Receptors α and β and Coregulators

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Supplementary Figure Legends and Table Titles

Supplementary Figure 1. Western blot showing presence of ERα and/or ERβ in ERα, ERα/ERβ, and ERβ MCF-7 cells. Cells treated with control vehicle (V) or 10 nM estradiol (E2) for 24 h before cell harvest and preparation of cell extracts. Equal amounts of protein were loaded per lane. β-actin is the internal loading reference.

Supplementary Figure 2. Categorization of binding sites into clusters based on colocalization of ERα, ERβ, RIP140, and SRC3, from our findings, and FOXA1 and GATA3, from data in Joseph et al, 2010 and Kong et al, 2011.

Supplementary Figure 3. RIP140 recruitment to various binding sites.

Supplementary Figure 4. RIP140 is required for E2 mediated cell proliferation in MCF-7 cells. **A.** Cell proliferation, **B.** FACS analysis and **C.** Gene expression analysis for G2/M associated genes in the three different cell backgrounds (ERα, ERα/ERβ and ERβ cells), which were wild type (siCtrl cells) or RIP140 depleted using shRNA (siRIP140 cells).

Supplementary Figure 5. Hierarchical clustering of gene expression values for G2/M activators and G2/M inhibitors in the three different cell backgrounds.

Supplementary Figure 6. Binding sites for ERα, ERβ, RIP140 and SRC3 for adipogenesis-associated genes studied in Figure 6.

Supplementary Figure 7. Impact of SRC3 or RIP140 knockdown on gene expression or recruitment of each coregulator to binding sites for adipogenesis genes DDIT3 and FOXO1A or pS2 and OTUB2.

Supplementary Figure 8. Impact of ERβ on **A.** Cell proliferation, **B.** Adipogenesis and **C.** Gene expression in T47D cells.

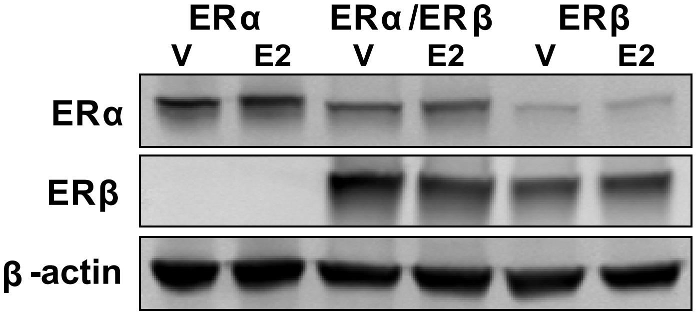
Supplementary Figure 9. Association of the ERβ and RIP140 gene signature with various concepts in tumor datasets.

Supplementary Figure 10. Association of the ERβ and RIP140 gene signature with clinical outcome in various breast cancer data sets. Using Oncomine concept maps, the ERβ/RIP140 gene signature was found to be significantly associated with outcome - metastasis, survival and recurrence- (yellow circles) in several data sets (red circles). Cytoscape software was used to generate the association map. Association P values were denoted on the edges for each data set and concept.

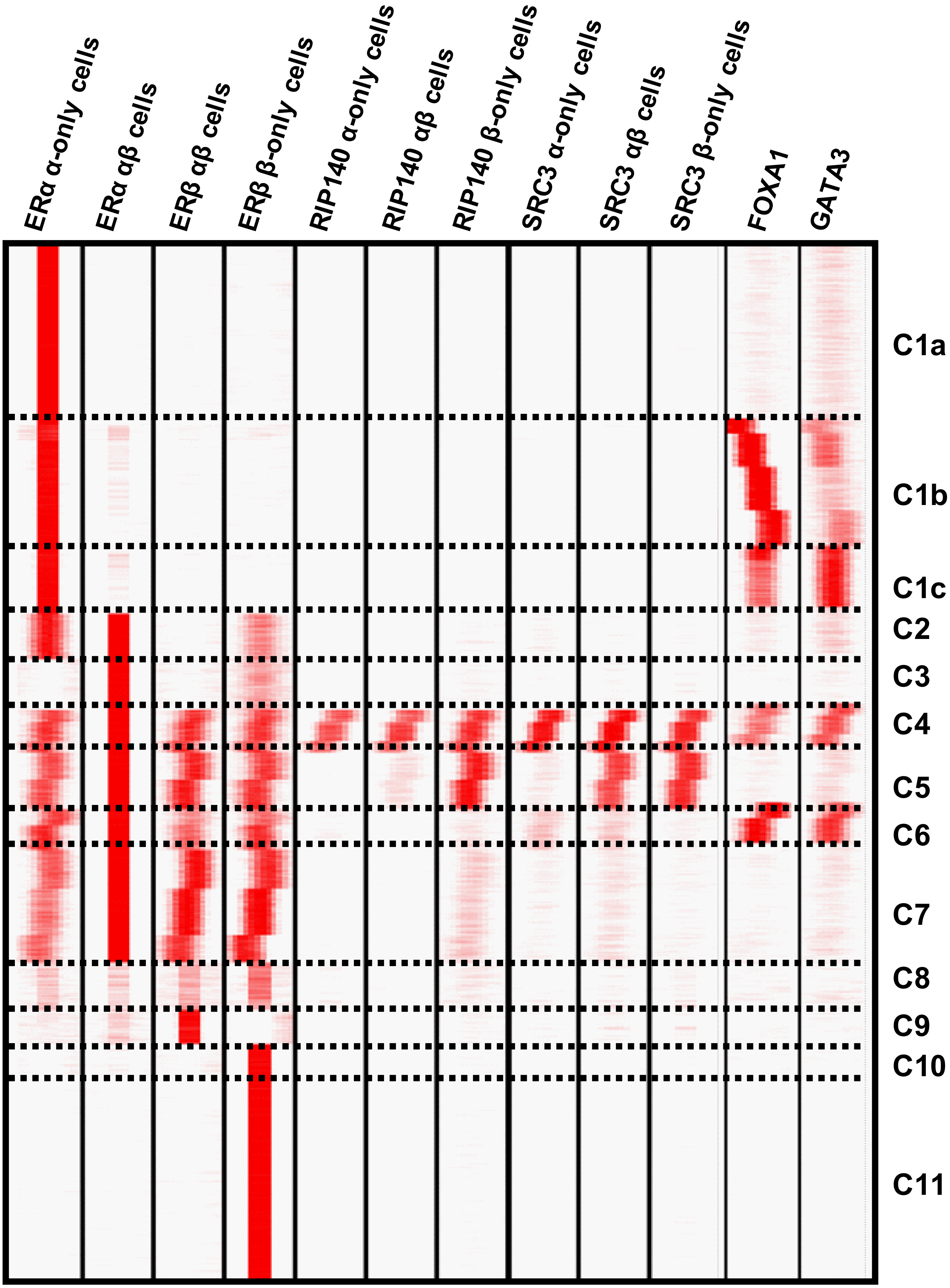
Supplementary Table 1. CEAS analysis of transcription factor binding motif enrichment for binding site clusters (C1-C11) identified through SeqMINER analysis.

Supplementary Table 2. SeqPos analysis of transcription factor binding motif enrichment for binding site clusters identified through SeqMINER analysis

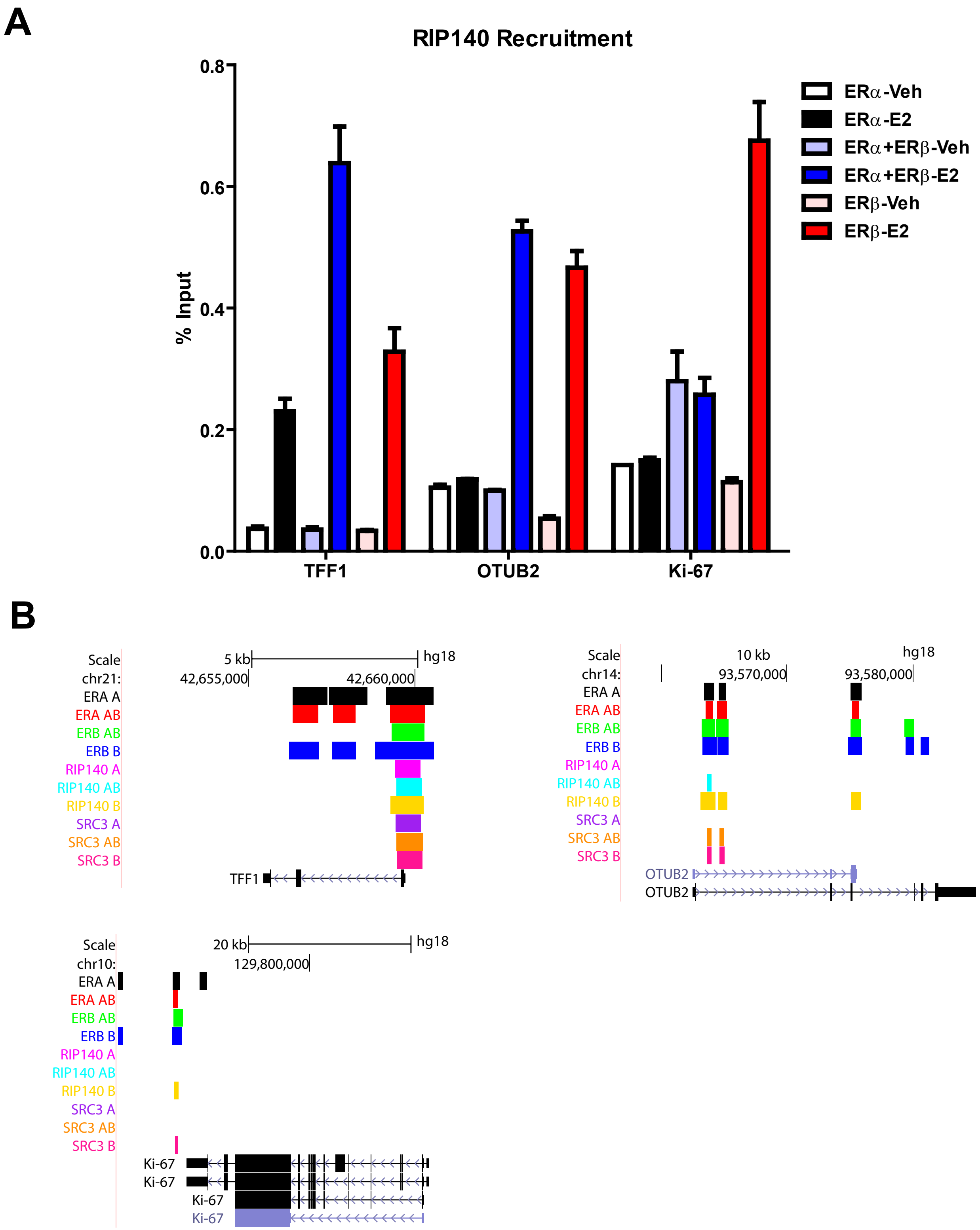
Supplementary Table 3. Functional enrichment of categories for ERβ-modulated genes. Enrichment by Pathway Maps; Enrichment by Process Networks; and Enrichment by Molecular Networks are shown.



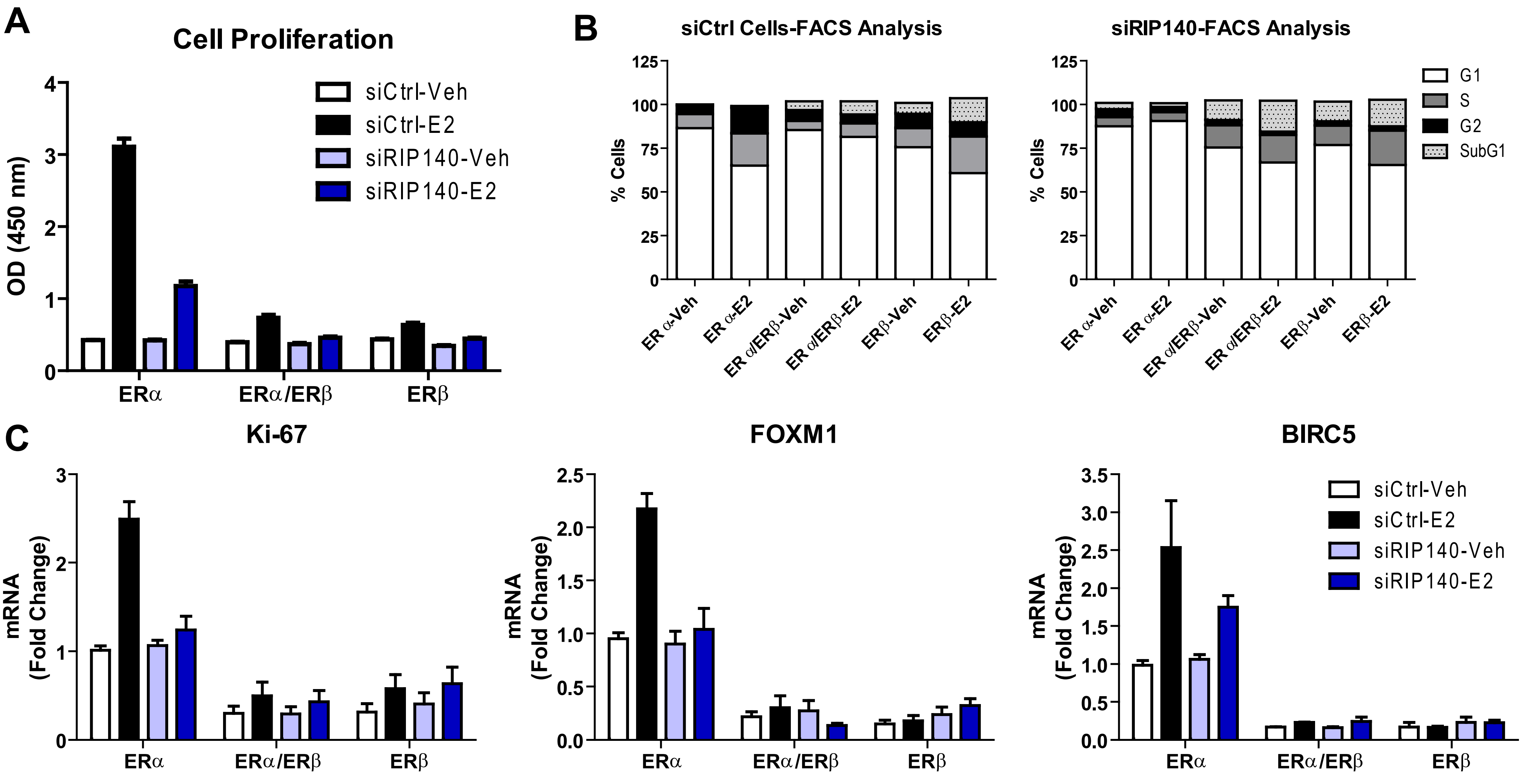
Supplementary Figure 1



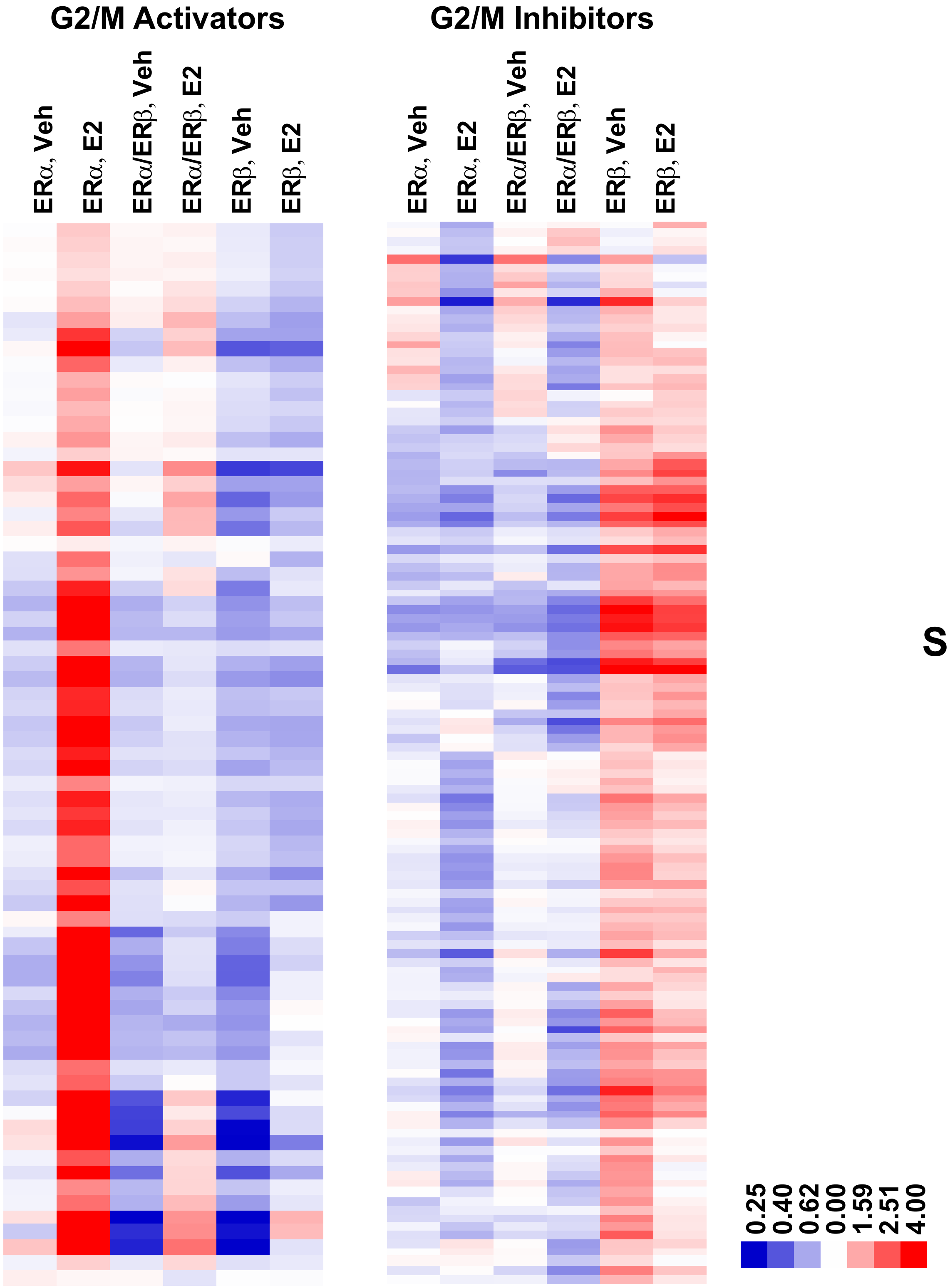
Supplementary Figure 2



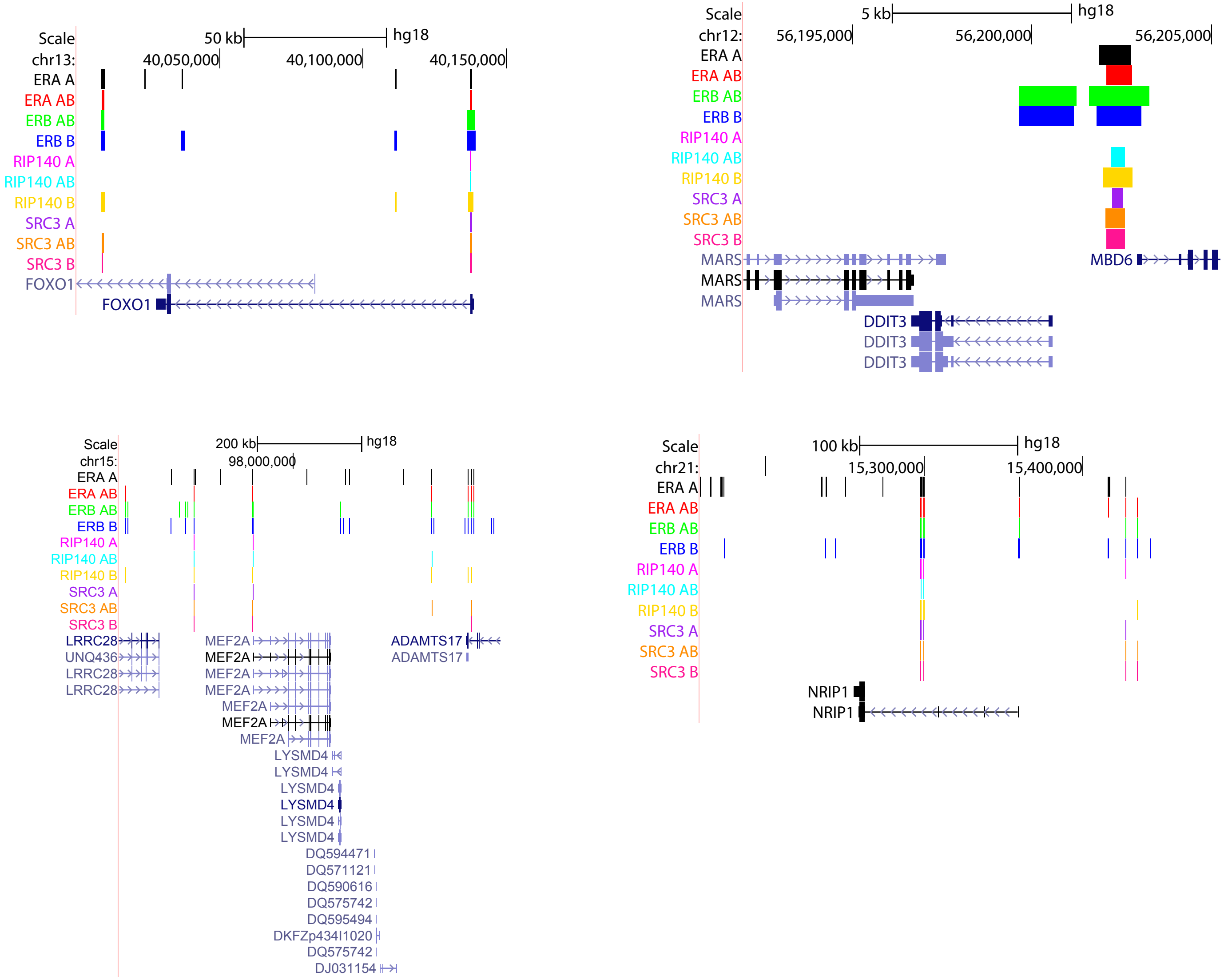
Supplementary Figure 3



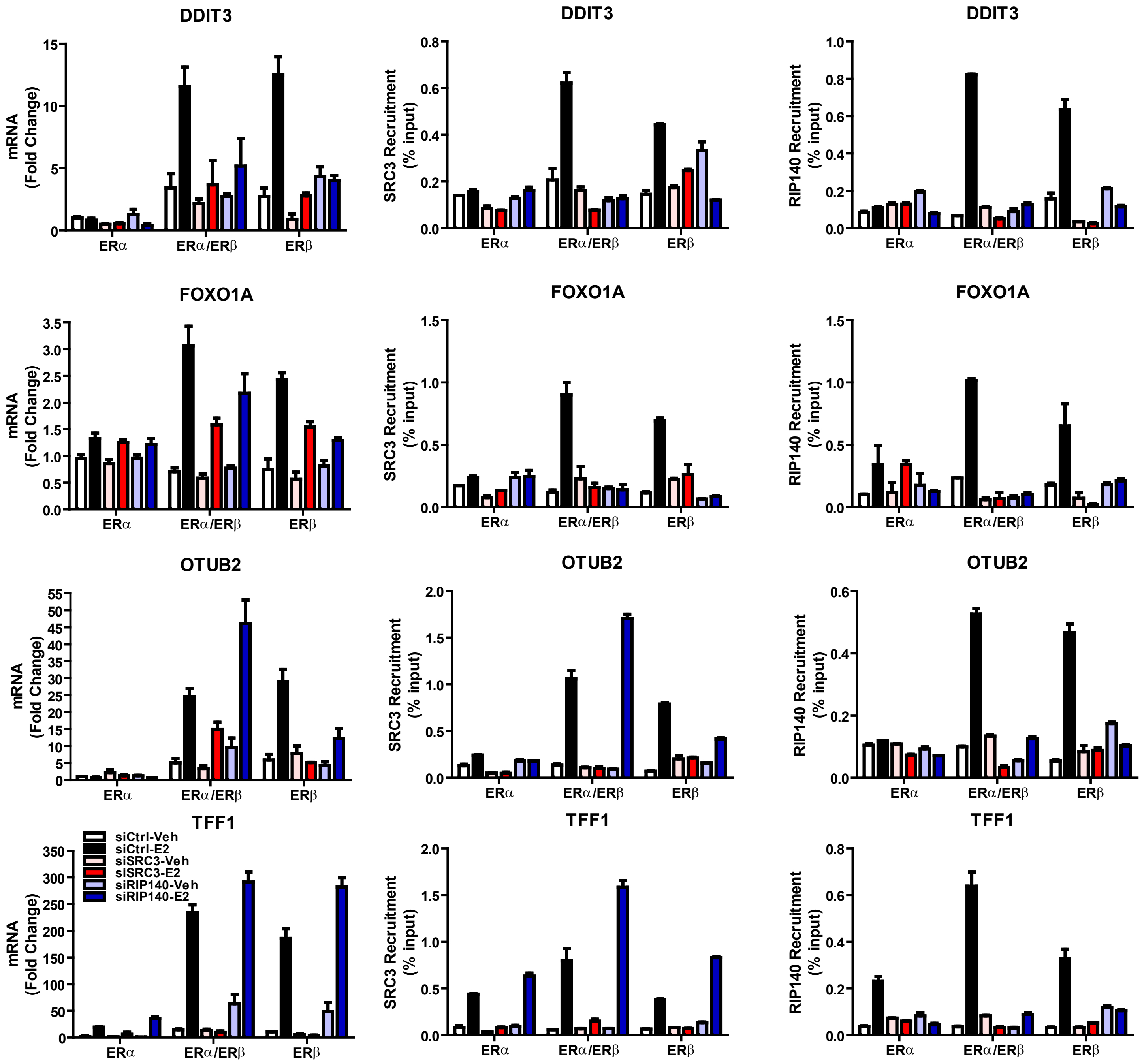
Supplementary Figure 4



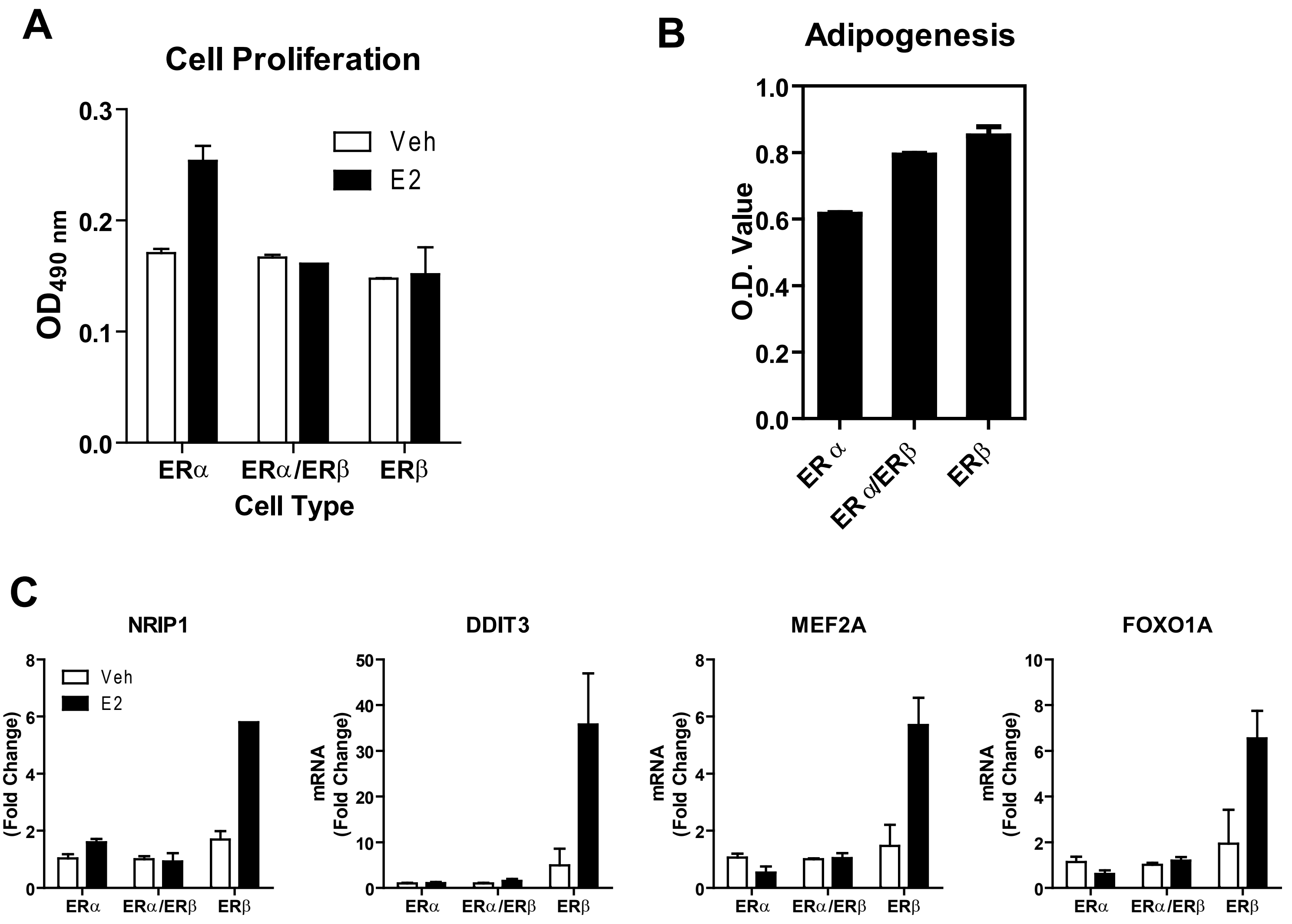
Supplementary Figure 5



Supplementary Figure 6



Supplementary Figure 7



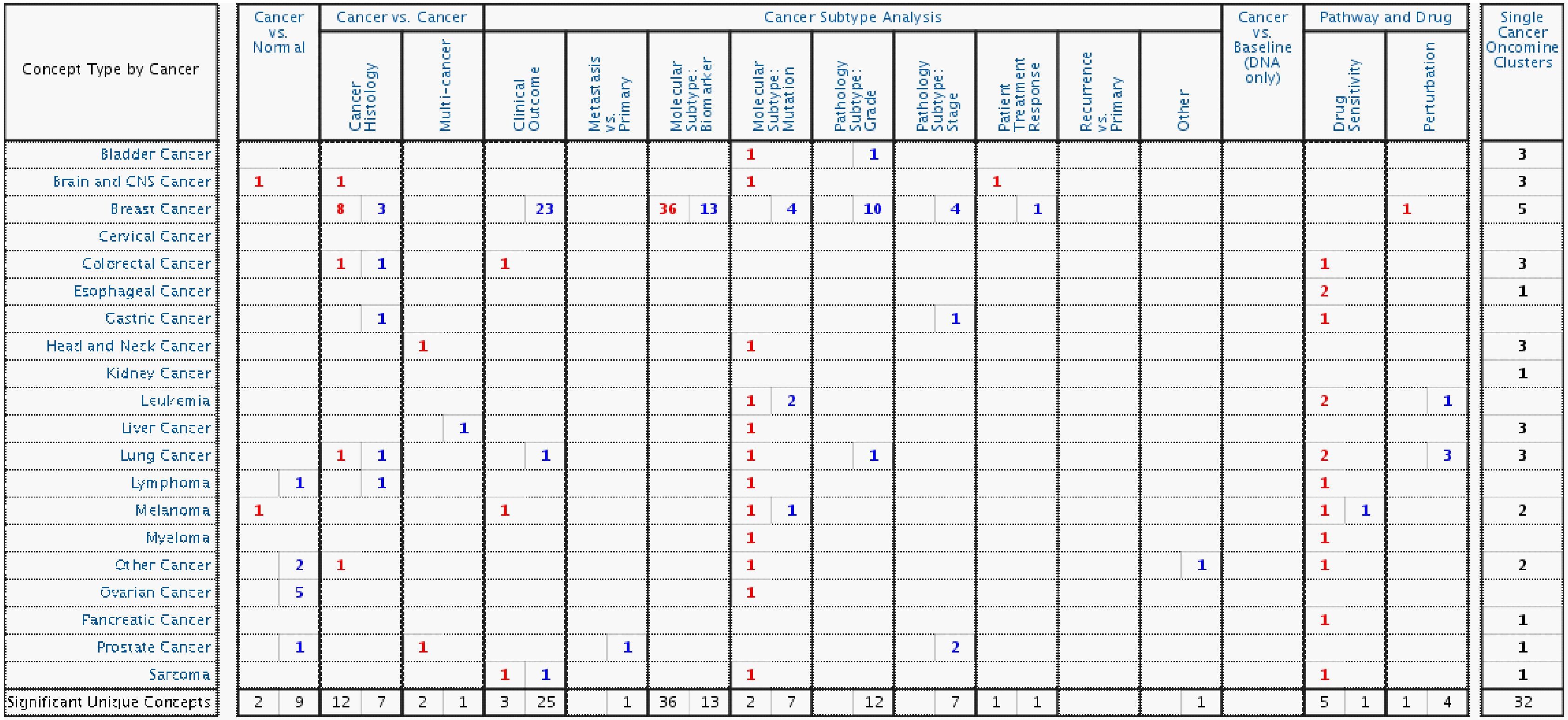
Supplementary Figure 8

ONCOMINE™

Associated Concept Summary for "NRIP1sig - My Concepts"

Threshold (Odds Ratio): 2.0 Threshold (P-value): 1E-4 Data Type: All

Oncomine Concept Summary



Concept Type by Cancer	Cancer vs. Normal		Cancer vs. Cancer				Cancer Subtype Analysis																		Cancer vs. Baseline (DNA only)		Pathway and Drug				Single Cancer Oncomine Clusters
			Cancer Histology		Multi-cancer		Clinical Outcome		Metastasis vs. Primary		Molecular Subtype: Biomarker		Molecular Subtype: Mutation		Pathology Subtype: Grade		Pathology Subtype: Stage		Patient Treatment Response		Recurrence vs. Primary		Other				Drug Sensitivity		Perturbation		
Bladder Cancer													1			1															3
Brain and CNS Cancer	1		1										1						1												3
Breast Cancer			8	3				23			36	13		4		10		4		1									1		5
Cervical Cancer																															
Colorectal Cancer			1	1			1																				1				3
Esophageal Cancer																											2				1
Gastric Cancer				1														1									1				
Head and Neck Cancer					1								1																		3
Kidney Cancer																															1
Leukemia													1	2													2			1	
Liver Cancer						1							1																		3
Lung Cancer			1	1				1					1			1											2			3	3
Lymphoma		1		1									1														1				
Melanoma	1						1						1	1													1	1			2
Myeloma													1														1				
Other Cancer		2	1										1											1			1				2
Ovarian Cancer		5											1																		
Pancreatic Cancer																											1				1
Prostate Cancer		1			1					1								2													1
Sarcoma							1	1					1														1				1
Significant Unique Concepts	2	9	12	7	2	1	3	25		1	36	13	2	7		12		7	1	1				1			5	1	1	4	32

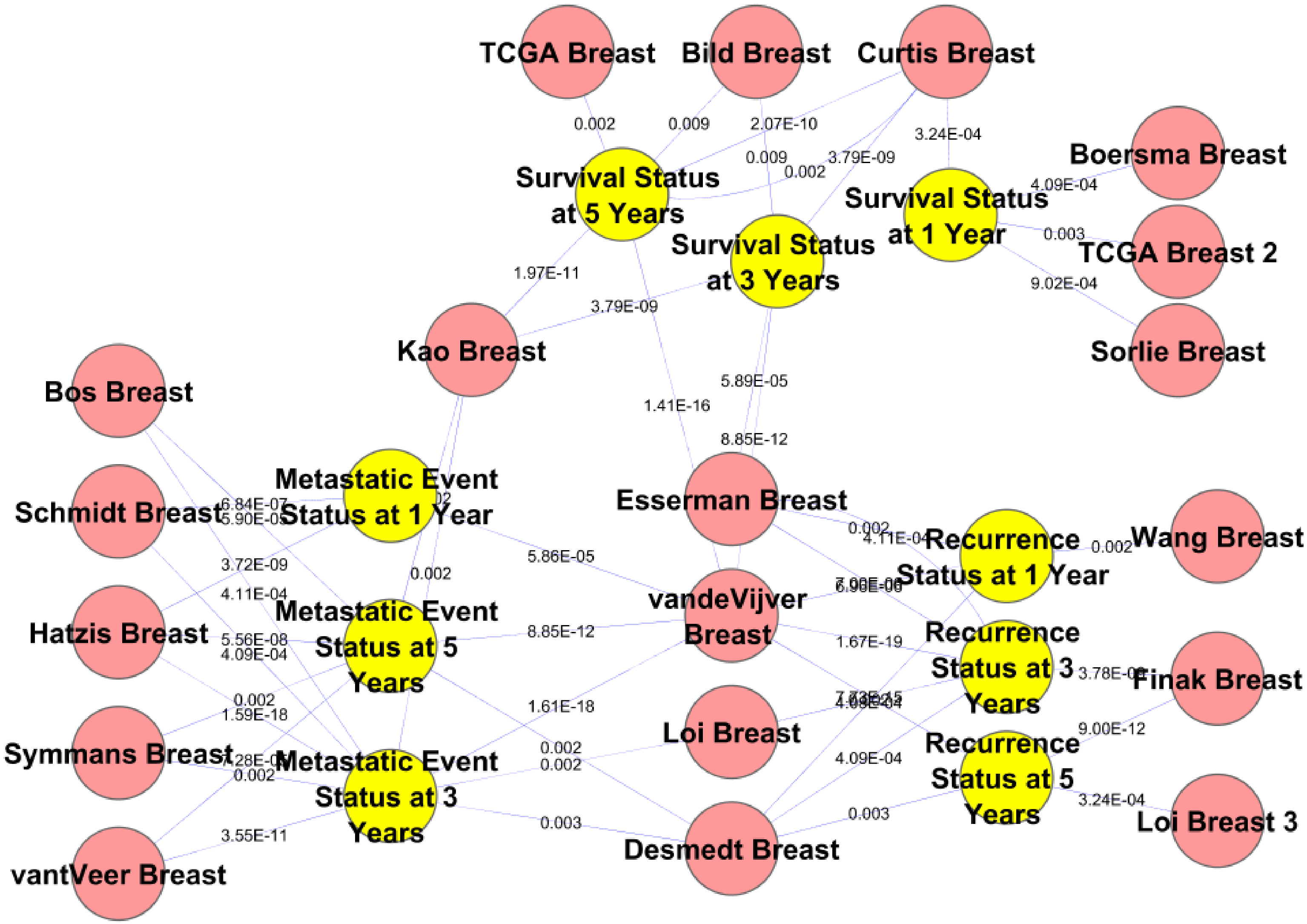
Red: Over-expression Blue: Under-expression

Other (Non-Oncomine) Concept Summary

Biological Annotations	Pathway Concepts	Regulatory Concepts	Connectivity Map v2 Drug Signatures	Literature-defined Concepts	Mutation Concepts	My Concepts	shRNA Concepts
		1	12	6		1	

Oncomine Source:
https://www.oncomine.com/resource/main.html#cc:122202926,19866,31124,122202938,28380,122196695,28428,28404,28459;cso:pvalue;cv:association;dso:geneUnderex;ec:[2,5];epv:108715,3508;et:under;pg:1;pvf:C30743;scr:conceptSummary;v:16

Supplementary Figure 9



Supplementary Figure 10