

Supplemental Figure 1 Uterine deletion of ER α

ER α immunohistochemistry of representative sections from *Esr1^{ff}* and *Esr1^{ff};Pgr^{Cre+}*(ER α UtcKO) uterine tissue. White bar=60 μ M

Supplemental Figure 2 Hierarchical Cluster

Cluster comparing all DE genes from WT, ER α UtcKO and Ex3 α ERKO samples treated with V, E2 or IGF1 for 2 hours or 24 hours. Yellow boxes indicate E2 selective DE genes.

Supplemental Figure 3 Pathway analysis of ER α -independent and dependent transcripts

- A) Pathway analysis of ER α independent transcripts. Biological functions (left) and upstream regulators (right) significantly enriched in the transcripts selected in 3A. Visualizations show activation Z scores. Blue=predicted inhibition; orange=predicted activation
- B) Pathway analysis of ER α dependent transcripts. Biological functions (left) and upstream regulators (right) significantly enriched in the transcripts selected in 4A. Visualizations show the activation Z scores. Blue=predicted inhibition; orange=predicted activation

Supplemental Figure 4 Examples of ER α ChIP-seq and RNA-seq of ER α -independent and dependent genes

- A. UCSC Genome Browser visualization of four ER α dependent genes (*Dhcr24*, *Wnt4*, *Ngfr* and *Map2k6*). Each panel includes four ER α ChIP-seq tracks (Vehicle (V), 1h E2, 1h IGF1 and 1h ICI) below the Refseq transcript track. Below are RNA-seq tracks from saline vehicle (V) or E2 2h samples. Boxes indicate peaks of E2 or IGF1 dependent ER α binding. Dashed arrows indicate transcription direction.

- B. Venn diagram comparing the 1724 TSS closest to overlapping E2 and IGF1 ER α ChIP-peaks and the 262 coding RNA transcripts from the 654 transcripts selected in Fig. 3A. Genes listed did not overlap with E2 and IGF1 ER α binding sites and were tested by RT-PCR.
- C. UCSC Genome Browser visualization of three ER α independent genes (*Fos*, *Adamts5*, and *Ppargc1a*). Each panel includes four ER α ChIP-seq tracks (Vehicle (V), 1h E2, 1h IGF1 and 1h ICI) below the Refseq transcript track. Below are RNA-seq tracks from vehicle (V) or E2 2h samples. For *Fos*, potential ER α -independent sites are indicated, where E2, but not IGF1 increases ER α binding.

Supplemental Table 1: RNA samples used in microarray study

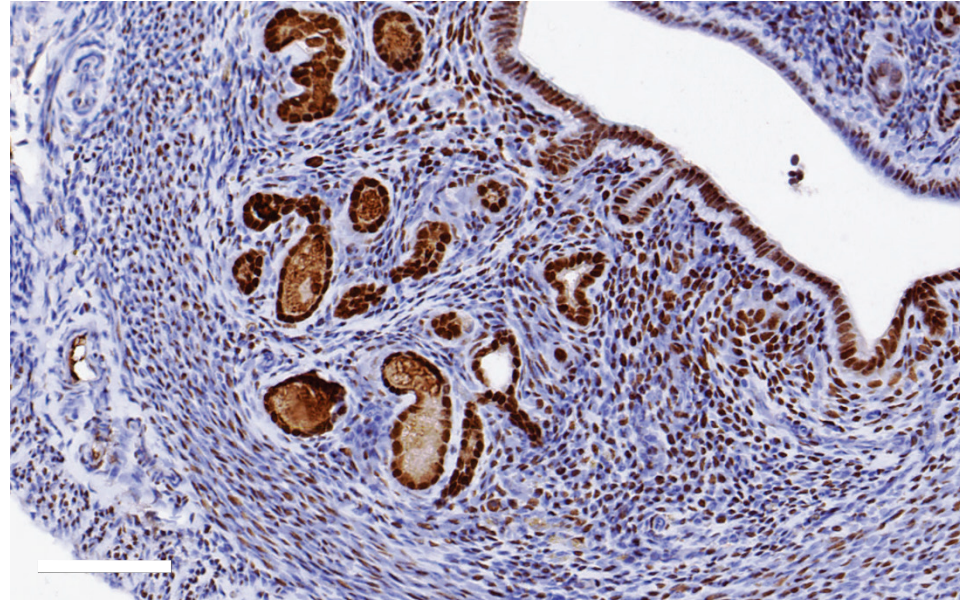
Samples tested	WT	Ex3αERKO (global ERα-null)	ERαUtcKO (uterine ERα-null)
V (Saline)	n=8	n=2	n=3
E₂ (2h, 24h)	n=9,9	n=2,2	n=3,3
IGF1 (2h, 24h)	n=7,9	n=2,3	n=3,3

Table S2 Sequences of RT-PCR primers

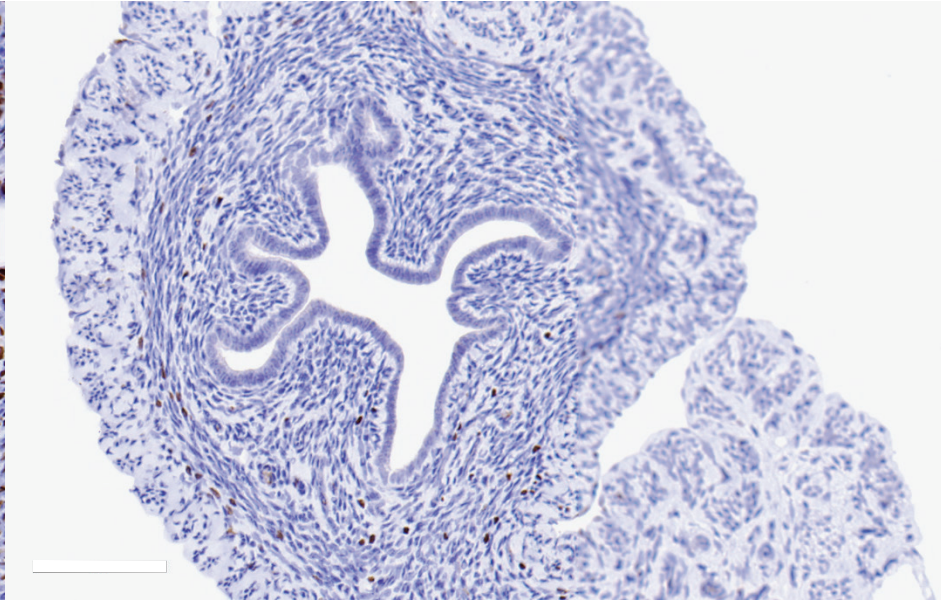
Gene	Forward Primer	Reverse Primer
<i>Adamts5</i>	GTGGGAAGGGAAGAGTCTGC	ACCCCAATTTCCATGGCTT
<i>Cdkn1a</i>	CAGCGACCATGTCCAATCC	CGAAGAGACAACGGCACACTT
<i>Dhcr24</i>	GACACCAAGAAACAGATTGTTCGA	TGGAGTTCAGCAAAGCTGTCA
<i>Fos</i>	GGAATGGTGAAGACCGTGTC	CCTCTTCAGGAGATAGCTGCTCTAC
<i>Map2k6</i>	GCTCCCAGCAGACAAGTTCT	TCTGGATATGTGGGCCGTTT
<i>Ngfr</i>	CGCTGACAACCTCATTCT	GCAGCTGTTCCATCTCTTGA
<i>Nr4a1</i>	GGGCATGGTGAAGGAAGTTGT	GAGGCTGCTTGGGTTTTGAA
<i>Ppargc1a</i>	AAGGTCCCCAGGCAGTAGAT	AAGGGAGAATTGCGGTGTGT
<i>Sox4</i>	GGCCCATGAACGCCTTT	TCGGGCGACTGCTCCAT
<i>Txnip</i>	ACCACTTTCTCGGATGTTGGA	GGAAAGACAACGCCAGAAGGT
<i>Wnt4</i>	AGTGACAAGGGCATGCAGC	CATCCTGACCACTGGAAGCC

Supplemental Figure 1

Esr1^{f/f}

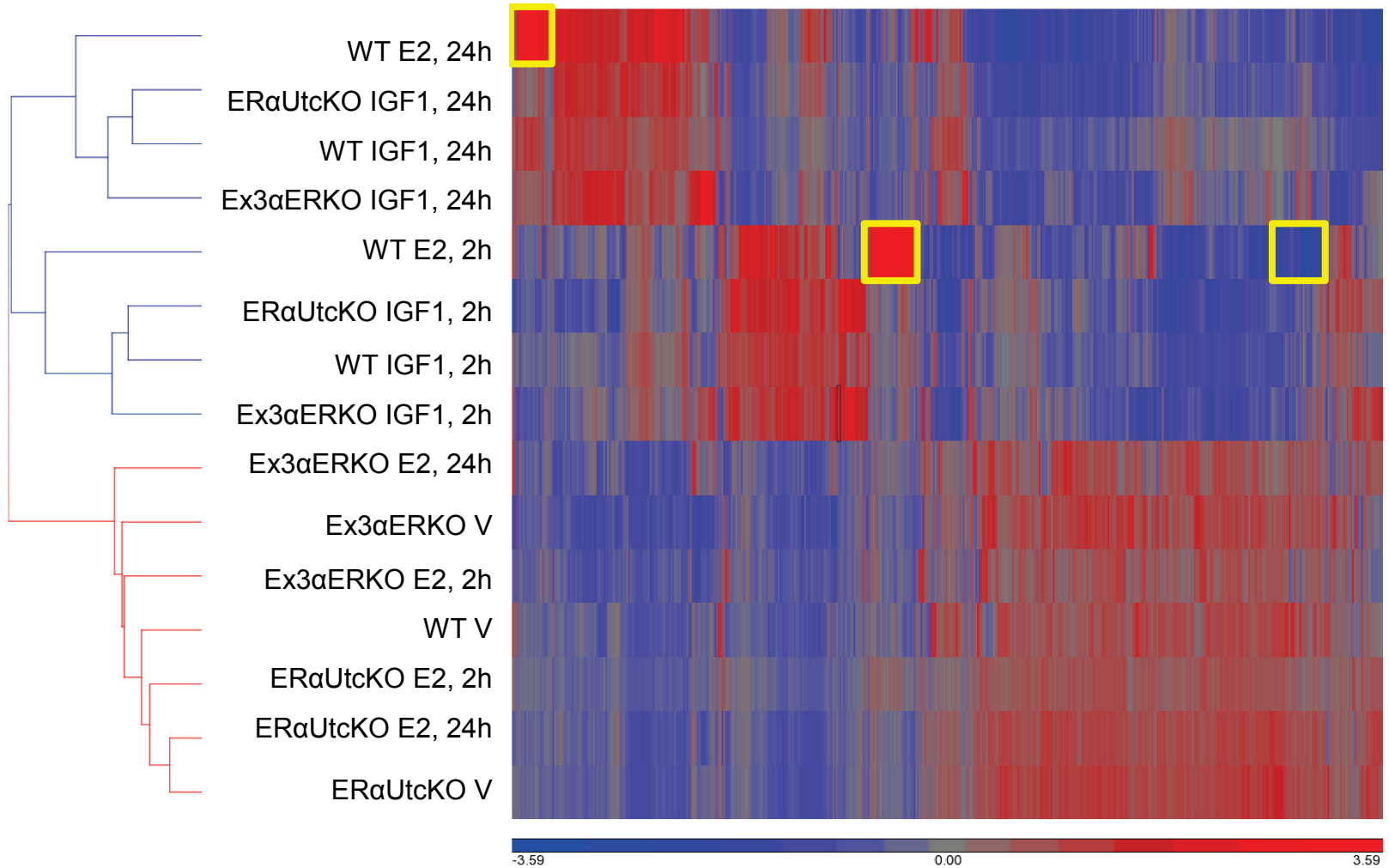


ER α UtcKO
(*Pgr*^{Cre+}; *Esr1*^{f/f})



Supplemental Figure S2

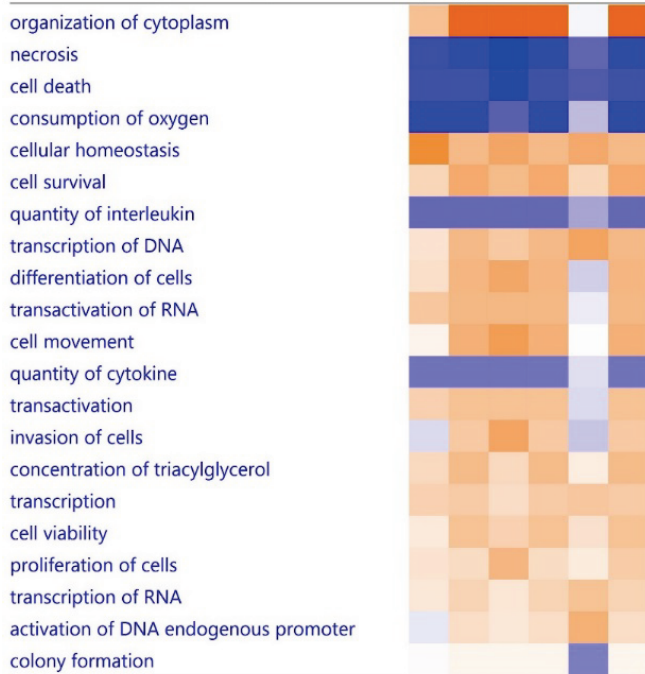
12000 DE probes log2 Intensities



Supplemental Figure 3A

ER Independent

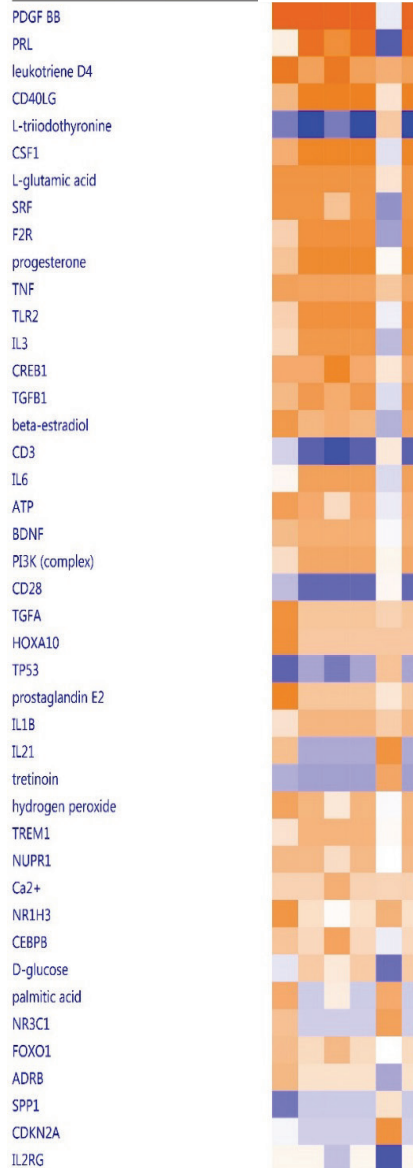
Diseases and Bio Functions



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ER Independent

Upstream regulators



Supplemental Figure 3B

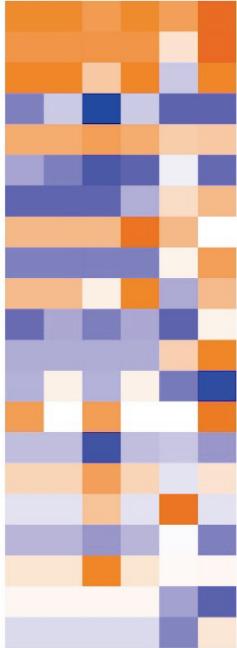
ER dependent/involved

Diseases and Bio Functions



- proliferation of cells
- activation of cells
- synthesis of steroid
- secretion of molecule
- migration of cells
- cell death
- fatty acid metabolism
- biosynthesis of hydrogen peroxide
- transport of lipid
- synthesis of lipid
- transport of molecule
- export of lipid
- secretion of lipid
- conversion of lipid
- necrosis
- cell survival
- cell cycle progression
- concentration of lipid
- cell viability
- quantity of steroid
- ion homeostasis of cells

WT E2 2h/V
 WT IGF1 2h/V
 ERα UtcKO E2 2h/V
 ERα UtcKO IGF1 2h/V
 Ex3αERKO E2 2h/V
 Ex3αERKO IGF1 2h/V



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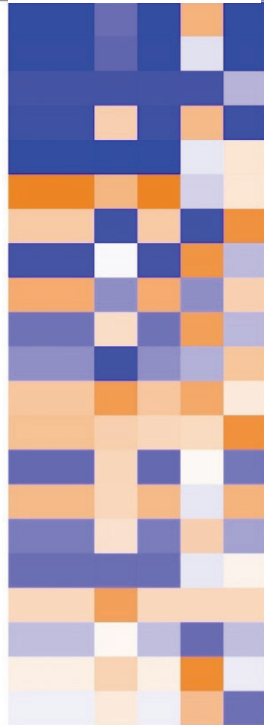
ER dependent/involved

Upstream regulators



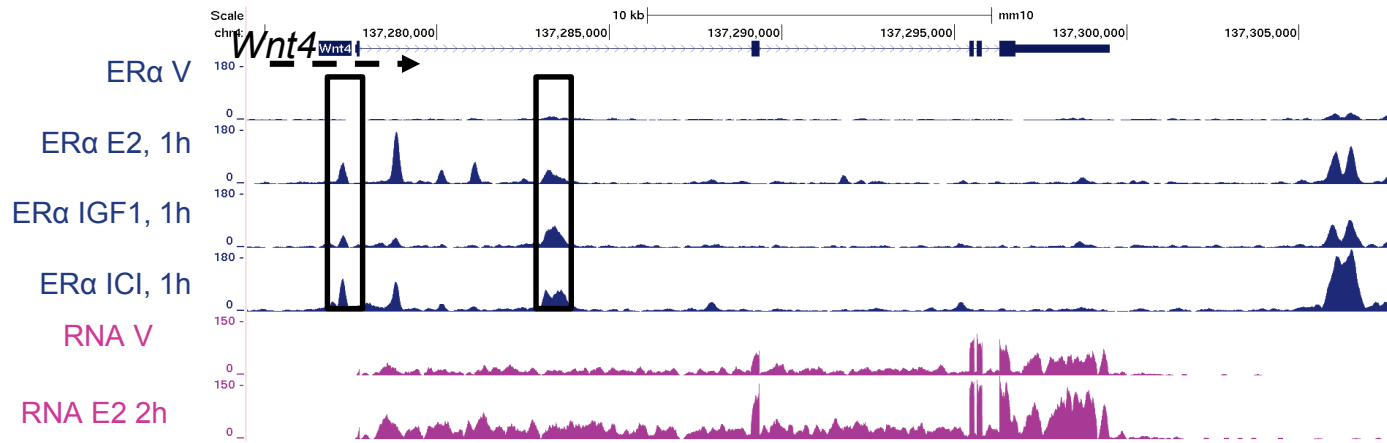
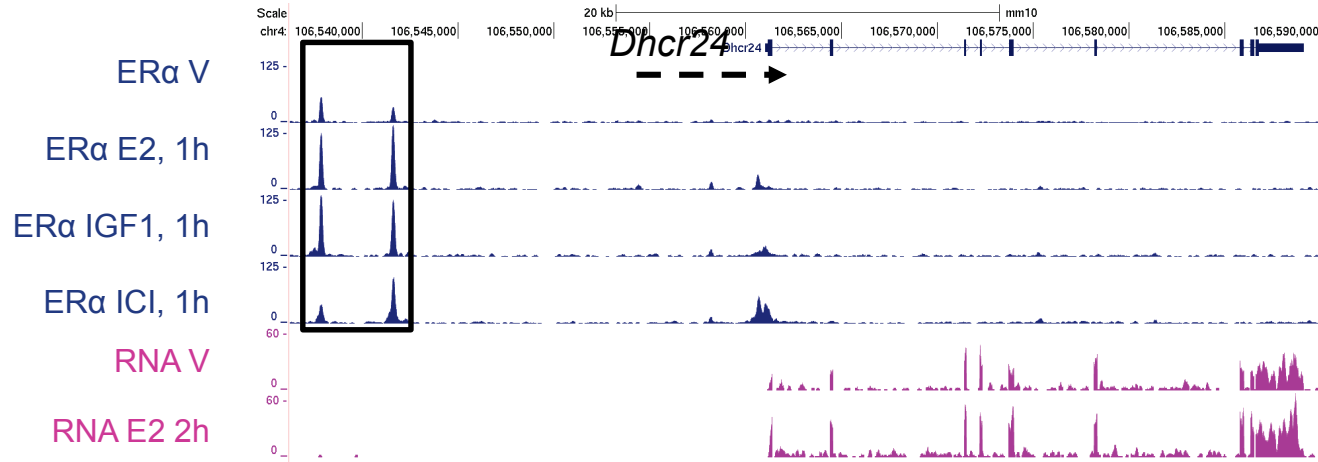
- CD28
- TP73
- LIF
- tretinoin
- HNF1A
- SOX2
- FGF2
- PPARG
- IL1
- IFNG
- L-triiodothyronine
- TGFB1
- beta-estradiol
- IL1B
- MYC
- KLF4
- OSM
- AR
- TP63
- TP53
- TNF

WT E2 2h/V
 WT IGF1 2h/V
 ERα UtcKO E2 2h/V
 ERα UtcKO IGF1 2h/V
 Ex3αERKO E2 2h/V
 Ex3αERKO IGF1 2h/V

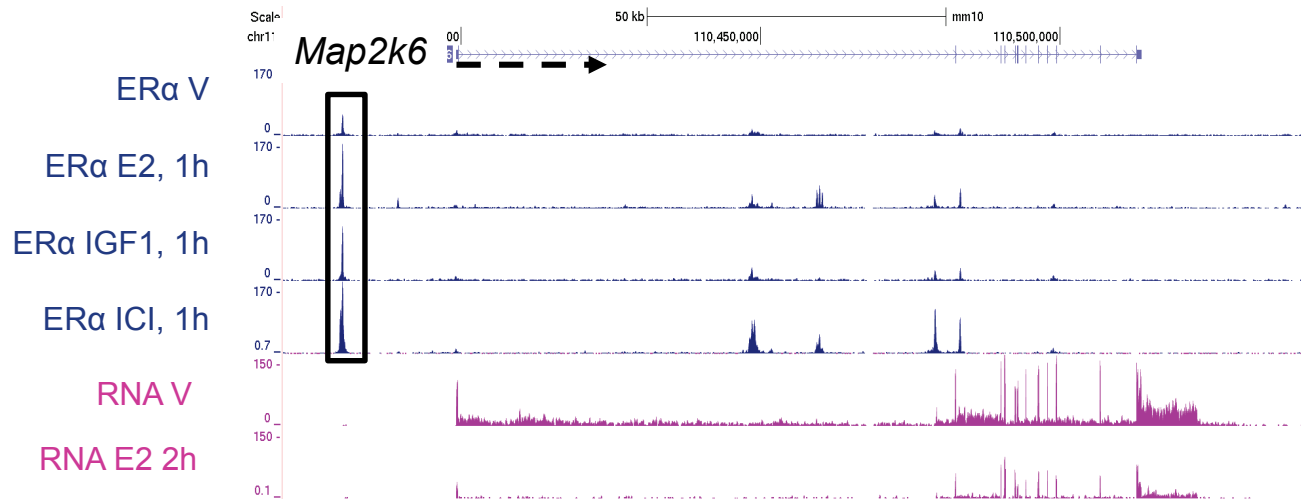
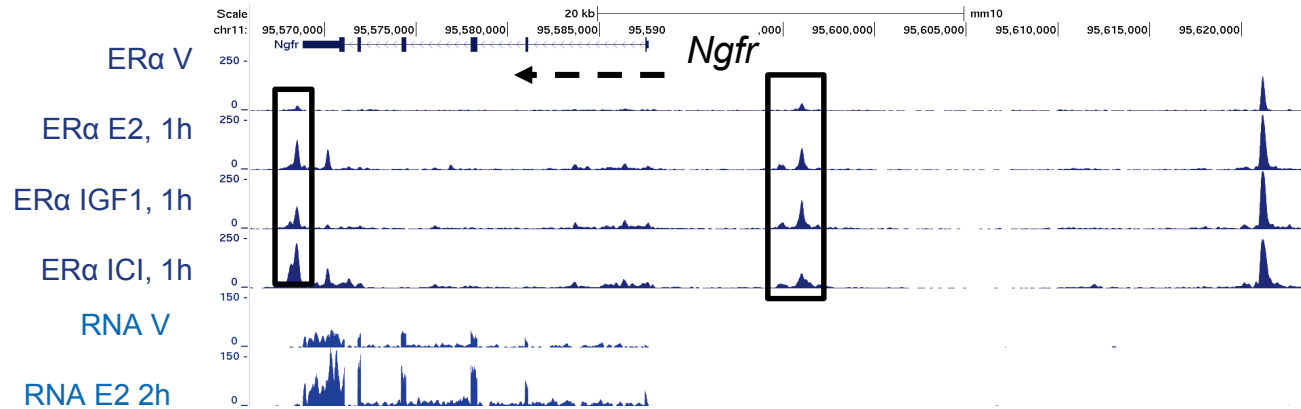


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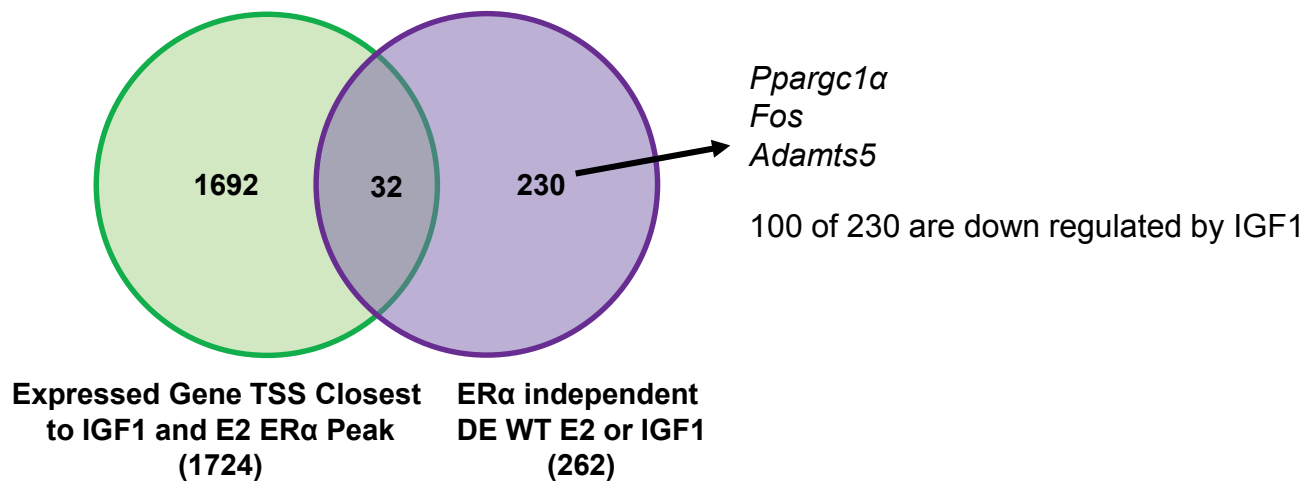
Supplemental Figure 4A

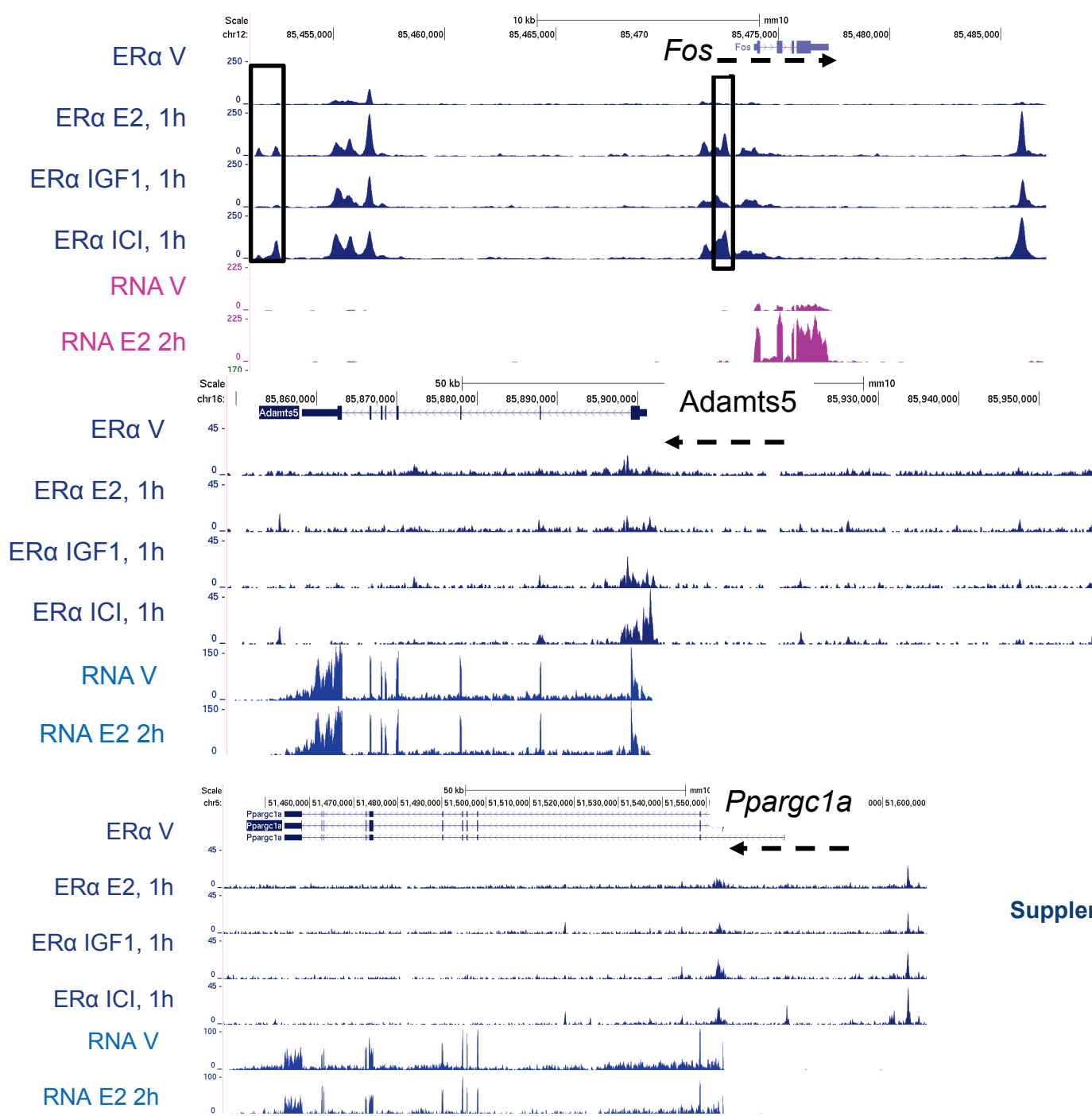


Supplemental Figure 4A



Supplemental Figure 4B





Supplemental Figure 4C