

Figure S1: mRNAs were isolated from ER α -transduced endothelial cells treated by E2, TAM or the combination of E2+TAM compared to vehicle (DMSO) and sequenced. (A) Relative expression of ESR1 mRNA in TeloHAEC cells transduced with the human ESR1 gene following the different treatments, (B) PCA demonstrated the source of variance in our data following the different treatments, showing that Tam and E2+Tam are quite similar as opposed to E2 and vehicle. (C-D) Heat-map representative of the differentiated genes in the Estrogen Early response and Estrogen late response pathway identified from GSEA. Statistical relevance was measured by Kruskal-Wallis followed by Dunn's post test and is represented as follows: **P*<0.05, for the control *vs*. treated groups comparisons in hER α -WT cell line.

Figure S2: Relative expression of angiogenic and cell metabolism mRNAs in TeloHAEC cells transduced or not with the human ESR1 gene following the different treatments (n = 5-6 per group from 2 independent experiments). Statistical relevance was measured by one-way ANOVA followed by Bonferroni post test and is represented as follows: * P<0.05, ** P<0.01, ***P<0.001, ***P<0.0001 for the control *vs.* treated groups comparisons; and (\$\$ P<0.01, \$\$\$ P<0.001) for the comparisons between the 4-OHT or E2+4-OHT *vs.* E2 conditions.

Figure S3: Relative mRNA levels of NR2F6, NR2F2, ETS2, SMAD1, SMAD6 and FOXC1 transcription factors in TeloHAEC transduced or not with the human ESR1 gene following the different treatments (n =6 per group from 2 independent experiments). Statistical relevance was measured by two-way ANOVA followed by Bonferroni's post test. : * P < 0.05, ** P < 0.01, ***P < 0.001, ****P < 0.0001 for the control *vs.* treated group comparisons; and (\$\$ P < 0.01, \$\$\$ P < 0.001) for the comparisons between the 4-OHT or E2+ 4-OHT *vs.* E2 conditions.

Gene symbol	NCBI Reference Sequence	Species	Forward Sequence (5'-3')	Reverse Sequence (5'-3')
ESR1	NM_000125	Homo Sapiens	GAGTCTGGTCCTGTGAGGGCT	TGGTTGGTGGCTGGACACATA
VEGFA	NM_001171623	Homo Sapiens	TGCTGTCTTGGGTGCATTGGA	CCACTTCGTGATGATTCTGCC
HEY2	NM_012259	Homo Sapiens	ACGACCTCCGAGAGCGACAT	ATCCGATCCCGACGCCTTTTC
DLL4	NM_019074	Homo Sapiens	CTGTGCCAACGGGGGGACAGTG	GTGGGCGCAAGGGTTACGGG
PFKFB3	NM_004566	Homo Sapiens	CCGAGTGCAGAAGATCTGGGT	TGGGGGAGTTGGTCAGCTTTG
GLUT1	NM_006516	Homo Sapiens	CCCTGCAGTTTGGCTACAACA	ATAGCGGTGGACCCATGTCTG
PDK4	NM_002612	Homo Sapiens	GCCTGTGAGACTCGCCAACAT	GCTTTCTGGTCATCTGGGCTTTT
MPC1	NM_016098	Homo Sapiens	CATGAGTACGCACTTCTGGGGC	AGTTCCGAGGCTGTACCTTGT
HPRT	NM_000194	Homo Sapiens	TGCTTTCCTTGGTCAGGCAGT	CTTCGTGGGGTCCTTTTCACC
NR2F6	NM_005234	Homo Sapiens	CGGCAAGCATTACGGTGTCTT	ATCTGGCAGTCACGGTTGGAC
NR2F2	NM_021005	Homo Sapiens	AGGCCATAGTCCTGTTCACCTC	AAAGCTTTCCGAATCTCGTCGG
ETS2	NM_005239	Homo Sapiens	GCAGCGGCAGGATGAATGA	CCAAGCCTGTTGGCACTTCTT
SMAD1	NM_005900	Homo Sapiens	TCCCCTGCCCTCAGAAATCAA	CATGGAACGCTTCACCCACAC
SMAD6	NM_005585	Homo Sapiens	ACCTCCCTACTCTCGGCTGT	AGACATGCTGGCGTCTGAGAA
FOXC1	NM_001453	Homo Sapiens	TTCGAGTCACAGAGGATCGGC	CGGTACAGAGACTGGCTGGAA
VEGFR2	NM_002253	Homo Sapiens	CCCAGATGACAACCAGACGGA	GCCACAGACTCCCTGCTTTTG

<u>Table S1 :</u> : List of primers for RT-qPCR.

Table S2: Matrice TFs expression motifs							
Category	TF	FC E2	FC OHT				
All	EGR2	1.44301760835644	2.43652325515723				
All	EZH2	0.743958085909748	0.873715941217246				
All	FOS	0.964715101776263	1.05330035011308				
All	ZBTB7A	0.638236214989486	0.887048140986128				
All	POLR2A	0.652989162329787	0				
All	ATF3	0	0				
All	CTCF	0	0				
All	EP300	0	0				
All	ESRRA	0	0				
All	HDAC2	0	0				
All	IRF1	0	0				
All	MAZ	0	0				
All	MXI1	0	0				
All	NR2C2	0	0				
All	RAD21	0	0				
All	SP1	0	0				
All	WT1	0	0				
E2_only	ZNF503	1.14832308897238	1.90477969349746				
E2_only	FOSB	1.0247636900742	1.01316623642807				
E2_only	JUNB	0.992384839139608	0.965347662654313				
E2_only	PPARA	0.98215458456039	0				
E2_only	PPARD	0.620800809642421	0				
E2_only	AKR1A1	0	0				
E2_only	ASCL1	0	0				
E2_only	BACH2	0	0				
E2_only	BATF	0	0				
E2_only	CTCFL	0	0				
E2_only	EBF1	0	0				
E2_only	EVX1	0	0				
E2_only	EVX2	0	0				
E2_only	FOSL1	0	0				
E2_only	FOSL2	0	0				
E2_only	GRHPR	0	0				
E2_only	GTF3C2	0	0				
E2_only	HAND1	0	0				
E2_only	HLCS	0	0				
E2_only	HNF4A	0	0				
E2_only	HNF4G	0	0				
E2_only	HSF4	0	0				
E2_only	HSPA1L	0	0				
E2_only	IKZF1	0	0				
E2_only	IRF2	0	0				
E2_only	IRF3	0	0				
E2_only	IRF4	0	0				
E2_only	IRF5	0	0				
E2_only	IRF6	0	0				
E2_only	IRF7	0	0				

		_	-
E2_only	IRF8	0	0
E2_only	IRF9	0	0
E2_only	JDP2	0	0
E2_only	KDM5A	0	0
E2_only	MTHFD1	0	0
E2_only	NANOG	0	0
E2_only	NFIA	0	0
E2_only	NFIB	0	0
E2_only	NFIX	0	0
E2_only	NFKB1	0	0
E2_only	NR1D1	0	0
E2_only	NR1H2	0	0
E2_only	NR1H3	0	0
E2_only	NR1H4	0	0
E2_only	NR1I2	0	0
E2_only	NR1I3	0	0
E2_only	NR2E3	0	0
E2_only	NR4A1	0	0
E2_only	NR4A2	0	0
E2_only	NR4A3	0	0
E2_only	NR5A1	0	0
E2_only	NR5A2	0	0
E2_only	NUP133	0	0
E2_only	PIR	0	0
E2_only	PPARG	0	0
E2_only	PRDM1	0	0
E2_only	RARA	0	0
E2_only	RBM17	0	0
E2_only	RNF114	0	0
E2_only	RORA	0	0
E2_only	RXRA	0	0
E2_only	RXRB	0	0
E2_only	RXRG	0	0
E2_only	SMAD2	0	0
E2_only	SMAD3	0	0
E2_only	SMAD4	0	0
E2_only	SMAD5	0	0
E2_only	SMAD9	0	0
E2_only	SMAP2	0	0
E2_only	SMARCC1	0	0
E2_only	SMC3	0	0
E2 only	SMPX	0	0
E2 only	STAT1	0	0
E2_only	STAT2	0	0
E2 only	STAT3	0	0
E2 only	TCEAL6	0	0
E2 only	THRA	0	0
E2 only	THRB	0	0
E2 only	TLX1	0	0
E2_only	TRIM21	0	0

E2 auto		0	0
E2_only		0	0
E2_OTHY		0	0
E2_OIIIy		0	0
E2_OIIIy		0	0
E2_only		0	0
E2_only	ZNF5/1	0	0
E2_only	ZNF595	0	0
E2_only	ZNF671	0	0
E2_only	ZNF71	0	0
E2_only	ZNF766	0	0
E2_only	SMAD1	0	-0.609981710518522
E2_only	SMAD6	0	-0.653329633302331
E2_only	MTA3	0	-0.862969779741773
E2_only	NR2F6	0	-0.953539304081849
E2_only	LTF	0	-1.27903625168257
OHT_only	TEF	1.11130304856721	0.62440889886011
OHT_only	ARID3A	0.864167319107167	0.673512686947838
OHT_only	FOXA1	0.883081087386496	0.668667643031372
OHT_only	FOXC1	0.874904220927108	0
OHT_only	TRPS1	0	0.738753974455545
OHT_only	TCF7L2	0	0.659821888662243
OHT_only	ATF2	0	0
OHT_only	BCLAF1	0	0
OHT_only	BHLHE40	0	0
OHT_only	CCNT2	0	0
OHT_only	CREB1	0	0
OHT_only	CUX1	0	0
OHT_only	DBP	0	0
OHT_only	E2F1	0	0
OHT_only	E2F6	0	0
OHT_only	FOXA2	0	0
OHT_only	FOXA3	0	0
OHT_only	FOXB1	0	0
OHT_only	FOXD1	0	0
OHT only	FOXD2	0	0
OHT only	FOXD3	0	0
OHT_only	FOXD4	0	0
OHT_only	FOXD4L1	0	0
OHT only	FOXD4L3	0	0
OHT_only	FOXD4L4	0	0
OHT only	FOXD4L5	0	0
OHT only	FOXD4L6	0	0
OHT only	FOXF2	0	0
OHT only	FOXL2	0	0
OHT only	FOXM1	0	0
OHT only	GATA1	0	0
OHT only	GATA3	0	0
OHT only	GATA4	0	0
OHT only	GATA5	0	0
OHT only	GATA6	0	0

OHT_only	GCM1	0	0
OHT_only	HCFC1	0	0
OHT_only	HIC1	0	0
OHT_only	HLF	0	0
OHT_only	KAT2A	0	0
OHT_only	MAX	0	0
OHT_only	MBD4	0	0
OHT_only	NFE2	0	0
OHT_only	NFIL3	0	0
OHT_only	NHLH1	0	0
OHT_only	PBX3	0	0
OHT_only	PHF8	0	0
OHT_only	REST	0	0
OHT_only	RUNX1	0	0
OHT_only	SIN3A	0	0
OHT_only	SOX8	0	0
OHT_only	TAF1	0	0
OHT_only	TBX15	0	0
OHT_only	TFAP2B	0	0
OHT_only	TRIM28	0	0
OHT_only	USF1	0	0
OHT_only	ZC3H11A	0	0
OHT_only	ZEB1	0	0
OHT_only	ZMIZ1	0	0
OHT_only	ZNF143	0	0
OHT_only	ZNF16	0	0
OHT_only	ZNF189	0	0
OHT_only	ZNF215	0	0
OHT_only	ZNF23	0	0
OHT_only	ZNF263	0	0
OHT_only	ZNF274	0	0
OHT_only	ZNF429	0	0
OHT_only	ZNF471	0	0
OHT_only	ZNF502	0	0
OHT_only	ZNF607	0	0
OHT_only	ZNF84	0	0
OHT_only	FOXC2	0	-0.854467281393582
OHT_only	MYC	0	-0.896244922724527
Common_E2_OHT	NXPH3	2.1675180632467	2.77857180621833
Common_E2_OHT	SIX2	1.31871763429417	1.61248549093675
Common_E2_OHT	SIX4	0	0.7869628524257
Common_E2_OHT	HOXB6	0	0.63057364100111
Common_E2_OHT	ISL2	0	0.64678158173597
Common_E2_OHT	ATF6	0	0
Common_E2_OHT	ATF6B	0	0
Common_E2_OHT	BSX	0	0
Common_E2_OHT	CDX1	0	0
Common_E2_OHT	CDX2	0	0
Common_E2_OHT	CDX4	0	0
Common_E2_OHT	CHURC1	0	0

Common_E2_OHT	CPSF4	0	0
Common E2 OHT	CREB3	0	0
Common E2 OHT	GPD1	0	0
Common E2 OHT	HOXA11	0	0
Common E2 OHT	HOXA13	0	0
Common E2 OHT	HOXA6	0	0
Common E2 OHT	HOXA7	0	0
Common F2 OHT	HOXB13	0	0
Common F2 OHT	HOXC11	0	0
Common F2 OHT	HOXC12	0	0
Common F2 OHT	HOXC13	0	0
Common F2 OHT	нохсе	0	0
Common F2 OHT		0	0
		0	0
	KI F1	0	0
	KLEIO	0	0
		0	0
	KLI 12 KI E15	0	0
		0	0
		0	0
		0	0
		0	0
		0	0
		0	0
Common_E2_OHT	KLF9	0	0
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		0	0
		0	0
	SALLZ	0	0
	SALL4	0	0
		0	0
		0	0
		0	0
Common_E2_OHT		0	0
		0	0
Common_E2_OHT	TEADO	0	0
Common_E2_OHT		0	0
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Common_E2_OHT		0	0
		0	U
		0	-0.580498280850372
Common_E2_OHT	KLF13	0	-0.59/31/245275044

Common_E2_OHT	KLF2	0	-0.631235538431652
Common_E2_OHT	KLF11	0	-0.752272135404255
E2_only_OHT_only	RCOR1	1.26209403280307	0
E2_only_OHT_only	EHF	0	0
E2_only_OHT_only	ELF1	0	0
E2_only_OHT_only	ELF2	0	0
E2_only_OHT_only	ELF3	0	0
E2_only_OHT_only	ELF4	0	0
E2_only_OHT_only	ELF5	0	0
E2_only_OHT_only	ELK1	0	0
E2 only OHT only	ELK3	0	0
E2 only OHT only	ELK4	0	0
E2 only OHT only	ERF	0	0
E2 only OHT only	ERG	0	0
E2 only OHT only	ETS1	0	0
E2 only OHT only	ETV1	0	0
E2 only OHT only	ETV2	0	0
E2 only OHT only	ETV3	0	0
E2 only OHT only	ETV4	0	0
E2 only OHT only	ETV5	0	0
E2 only OHT only	ETV6	0	0
E2_only_OHT_only	ETV7	0	0
E2_only_OHT_only	FFV	0	0
E2_only_OHT_only	FGF19	0	0
E2_only_OHT_only	GARPA	0	0
E2_only_OHT_only	GARPR1	0	0
E2_only_OHT_only		0	0
E2_only_OHT_only		0	0
E2_only_OHT_only	MVBL2	0	0
E2_only_OHT_only	NEIC	0	0
E2_only_OHT_only		0	0
		0	0
		0	0
		0	0
E2_ONIV_OHT_ONIV		0	0
E2_ONIV_OHT_ONIV		0	0
E2_ONIV_OHT_ONIV		0	0
		0	0
E2_only_OH1_only	GATAZ	0	-0.6968//3501292/2
E2_only_OH1_only	ETS2	0	-0.755323206591533
E2_only_OH1_only	FLI1	0	-1.18690661115943
E2_only_CommonE2_OHT	RARG	1.63882465275859	2.1883484431748
E2_only_CommonE2_OHT	VDR	1.32253996493298	1.90530649475913
E2_only_CommonE2_OHT	ESR1	0	0
E2_only_CommonE2_OHT	ESR2	0	0
E2_only_CommonE2_OHT	ESRRB	0	0
E2_only_CommonE2_OHT	ESRRG	0	0

E2_only_CommonE2_OHT	GLI1	0	0
E2_only_CommonE2_OHT	GLI2	0	0
E2_only_CommonE2_OHT	GLI3	0	0
E2_only_CommonE2_OHT	GLIS1	0	0
E2_only_CommonE2_OHT	GLIS2	0	0
E2_only_CommonE2_OHT	GLIS3	0	0
E2_only_CommonE2_OHT	KLF6	0	0
E2_only_CommonE2_OHT	MZF1	0	0
E2_only_CommonE2_OHT	NR2C1	0	0
E2_only_CommonE2_OHT	NR2F1	0	0
E2_only_CommonE2_OHT	PLAGL1	0	0
E2_only_CommonE2_OHT	PRDM16	0	0
E2_only_CommonE2_OHT	RARB	0	0
E2_only_CommonE2_OHT	ZIC1	0	0
E2_only_CommonE2_OHT	ZIC2	0	0
E2_only_CommonE2_OHT	ZIC3	0	0
E2_only_CommonE2_OHT	ZNF202	0	0
E2_only_CommonE2_OHT	NR2F2	0	-0.886391916250244
OHT_only_CommonE2_OHT	EGR3	1.78805085388839	1.7876688311356
OHT_only_CommonE2_OHT	SREBF1	0.591055015872863	0
OHT_only_CommonE2_OHT	EGR1	0	1.1248199410932
OHT_only_CommonE2_OHT	BRF1	0	0
OHT_only_CommonE2_OHT	BRF2	0	0
OHT_only_CommonE2_OHT	CEBPA	0	0
OHT_only_CommonE2_OHT	CEBPE	0	0
OHT_only_CommonE2_OHT	CEBPG	0	0
OHT_only_CommonE2_OHT	EGR4	0	0
OHT_only_CommonE2_OHT	KLF16	0	0
OHT_only_CommonE2_OHT	KLF3	0	0
OHT_only_CommonE2_OHT	NELFE	0	0
OHT_only_CommonE2_OHT	NFYB	0	0
OHT_only_CommonE2_OHT	PATZ1	0	0
OHT_only_CommonE2_OHT	POLR3G	0	0
OHT_only_CommonE2_OHT	RBBP5	0	0
OHT_only_CommonE2_OHT	SMARCA4	0	0
OHT_only_CommonE2_OHT	SP2	0	0
OHT_only_CommonE2_OHT	SP3	0	0
OHT_only_CommonE2_OHT	SP4	0	0
OHT_only_CommonE2_OHT	SREBF2	0	0
OHT_only_CommonE2_OHT	SUPT20H	0	0
OHT_only_CommonE2_OHT	XRCC4	0	0
OHT_only_CommonE2_OHT	ZBTB17	0	0
OHT_only_CommonE2_OHT	ZBTB7B	0	0
OHT_only_CommonE2_OHT	CEBPD	0	-0.872574287095308
OHT_only_CommonE2_OHT	CEBPB	0	-0.878845531863745

	Figure 1									
Figure ID	Normality	Test	Post-hoc test	Comparison	Summary	P-value	Sample size			
rigure ib	Normanty	105	i ostiloc test	Companson	Gainnary	I -Value	Group	n		
				P-interaction between Day and Treatment	****	<0.0001	ERα-WT OVX	12		
			Bonforroni'o multiplo	P Day	****	<0.0001	ERα-WT OVX+E2	10		
Figure 1B	YES	two-way ANOVA	comparisons test	P Treatment	****	<0.0001	ERα-AF1 ⁰ OVX	14		
							ERa-AF1" OVX+E2	14		
				P-interaction between Day and Treatment	****	<0.0001	ERα-WT OVX	16		
Figure 1C	VEC		Bonferroni's multiple	P Day	****	<0.0001	ERα-WT OVX+E2	12		
Figure 1C	TEO	two-way ANOVA	comparisons test	P Treatment	****	<0.0001	ERα-AF2 ⁰ OVX	15		
							ERα-AF2 ⁰ OVX+E2	16		
					**	0.007001	ERα-WT OVX	10		
Firme 4D	NO	Multiple Manage Militeres	Benjamini, Kriedger	ENG-WI OVX VS. ENG-WI OVX EZ		0.007331	ERα-WT OVX+E2	15		
Figure 1D	NU	wuitiple wann-whitney	and rekutiel post-		20	0.525070	ERα-AF1 ⁰ OVX	20		
			lesi	ERG-AF1 OVX VS. ERG-AF1 OVX+E2	115	0.555979	ERα-AF1 ⁰ OVX+E2	24		
				P-interaction between Day and Treatment	****	<0.0001	ERα-WT OVX	14		
Figure 1E	VES	two-way ANOVA	Bonferroni's multiple	P Day	****	<0.0001	ERα-WT OVX+E2	10		
riguie re	120	two way Alto VA	comparisons test	P Treatment	****	<0.0001	ERα-C451A OVX	13		
							ERα-C451A OVX+E2	14		
				P-interaction between Day and Treatment	****	<0.0001	ERa-WT OVX+Dendrimer	14		
Figure 1F	YES	two-way ANOVA	Bonferroni's multiple	P Day	****	<0.0001	ERα-WT OVX+E2	12		
riguio ii		the hay rate th	comparisons test	P Treatment	****	<0.0001	ERa-WT OVX+EDC	15		
				ERa-WT OVX+Dendrimer vs. ERa-WT OVX+E2	ns	0.5299	ERa-WT OVX+Dendrimer	25		
Figure 1G	NO	Kruskal-Wallis	Dunn's multiple	ERa-WT OVX+Dendrimer vs. ERa-WT OVX+EDC	*	0.0378	ERα-WT OVX+E2	48		
1.9210 10			comparisons test	ERa-WT OVX+E2 vs. ERa-WT OVX+EDC	\$\$\$\$	<0.0001	ERα-WT OVX+EDC	38		

	Figure 2									
Figure ID	Normality	Test	Post-hoc test	Comparison	Summary	P-value.	Sample size			
rigure ib	Normanty		1 Ost-noc test	Companson	Samaly	1-Value	Group	n		
			Denferrenile multiple	P-interaction between Day and Treatment	***	<0.0001	ERa-WT OVX	6		
Figure 2B	YES	two-way ANOVA	Bonferroni's multiple comparisons test	P Day	***	<0.0001	ERa-WT OVX+E2	5		
				P Treatment	****	<0.0001	ERα-WT OVX+TAM	8		
				P-interaction between Day and Treatment	****	<0.0001	ERa-WT OVX	16		
Figure 2D	VES	two-way ANOVA	Bonferroni's multiple	P Day	****	<0.0001	ERα-WT OVX+E2	6		
riguic 2D	120	two-way Artovia	comparisons test	P Treatment	***	<0.0001	ERa-WT OVX+TAM d4	22		
							ERα-WT OVX+E2+TAM d4	16		
				ERa-WT OVX versus ERa-WT OVX+E2	*	0.0353	ERa-WT OVX	3		
				ERa-WT OVX versus ERa-WT OVX+TAM d4	ns	>0.9999	ERa-WT OVX+E2	4		
Eiguro 2E	VES	'ES one-way ANOVA	Bonferroni's multiple comparisons test	ERa-WT OVX versus ERa-WT OVX+E2+TAM d4	ns	>0.9999	ERa-WT OVX+TAM d4	3		
rigule 21	1123			ERa-WT OVX+E2 versus ERa-WT+TAM d4	\$	0.0186	ERα-WT OVX+E2+TAM d4	5		
				ERa-WT OVX+E2 versus ERa-WT+E2+TAM d4	\$\$	0.0022		1		
				ERa-WT OVX+TAM d4 versus ERa-WT+E2+TAM d4	ns	>0.9999				
	re 2G YES one-way ANOV			ERa-WT OVX versus ERa-WT OVX+E2	**	0.0021	ERa-WT OVX	3		
				ERa-WT OVX versus ERa-WT OVX+TAM d4	***	0.0006	ERa-WT OVX+E2	4		
Figure 2G			Bonferroni's multiple	ERa-WT OVX versus ERa-WT OVX+E2+TAM d4	*	0.0235	ERa-WT OVX+TAM d4	3		
rigute 20		Une way Alto VA	comparisons test	ERa-WT OVX+E2 versus ERa-WT+TAM d4	ns	0.2041	ERα-WT OVX+E2+TAM d4	5		
				ERa-WT OVX+E2 versus ERa-WT+E2+TAM d4	ns	0.1486				
				ERa-WT OVX+TAM d4 versus ERa-WT+E2+TAM d4	†	0.0251		1		
			Ponforroni's multiple	P-interaction between Day and Treatment	*	0.0302	ERa-WT NT	8		
Figure 2I	YES	two-way ANOVA	comparisons tast	P Day	***	<0.0001	ERα-WT TAM d4	9		
			compansons test	P Treatment	*	0.0477				
				ERa-WT NT versus ERa-WT TAM d4	*	0.0109	ERa-WT NT	8		
Figure 2K	NO	Mann Whitney					ERα-WT TAM d4	5		
				ERa-WT NT versus ERa-WT TAM d4	ns	0.1274	ERa-WT NT	8		
Figure 2L	NO	Mann Whitney					ERα-WT TAM d4	5		

	Figure 3										
Figure ID Normality Tool	Test	Post-hoc test	Comparison	Summary	P-value.	Sample size					
rigure ib	rigue ib Normancy Teat	1 Ost-noc test	Companiaon	Summary	1-value	Group	n				
			ERa-WT OVX versus ERa-WT OVX+E2	•	0.0201	ERa-WT OVX	15				
			is Dunn's multiple comparisons test	ERa-WT OVX versus ERa-WT OVX+TAM	ns	>0.9999	ERa-WT OVX+E2	18			
Eigure 3C	NO	Kruekal-Wallie		ERa-WT OVX versus ERa-WT OVX+E2+TAM	**	0.0026	ERa-WT OVX+TAM	15			
rigute 50	NO	KTUSKal ^a VV aliis		ERa-WT OVX+E2 versus ERa-WT+TAM	ns	0.1486	ERa-WT OVX+E2+TAM	35			
				ERa-WT OVX+E2 versus ERa-WT+E2+TAM	\$\$\$\$	<0.0001					
		1	ERa-WT OVX+TAM d4 versus ERa-WT+E2+TAM	†††	0.0001						

				Figure 4				
Figure ID	Normality	Test	Post-hoc test	Comparison	Summarv	P-value	Sample	e size
3.0				5050			Group	n
			1	FGF2		1		
				DMSO versus E2	****	<0.0001	DMSO	6
		one-way ANOVA	Bonferroni's multiple	DMSO versus 4-OHT	**		E2	6
	YES			DMSO versus E2+4-OHT	ns	>0.9999	4-OHT	6
			comparisons test	E2 versus 4-OHI	\$\$\$\$	<0.0001	E2+4-0H1	6
				E2 Versus E2+4-OHI	\$\$\$\$	<0.0001		
				4-OHI versus E2+4-OHI	ns	0.0876		I
			1	VEGFA	***	0.0004	DMCO	6
				DMSO versus E2	****	<0.0004	DIVISO	6
	YES		Ponforroni'o multipla	DNISO Versus 4-OHT	****	<0.0001		6
		one-way ANOVA	comparisons test	E2 versus 4 OHT	2222	<0.0001	4-0HT	6
			oompanoono toot	E2 versus E2 4-OHT	\$\$\$\$	<0.0001	2214 0111	
				4-OHT versus E2+4-OHT	ps	>0.9999		-
				PDGFB	10			<u> </u>
				DMSO versus E2	ns	>0.9999	DMSO	6
				DMSO versus 4-OHT	****	<0.0001	E2	6
	1/50	4101/4	Bonferroni's multiple	DMSO versus E2+4-OHT	****	<0.0001	4-OHT	6
	TES	one-way ANOVA	comparisons test	E2 versus 4-OHT	\$\$\$\$	< 0.0001	E2+4-OHT	6
				E2 versus E2+4-OHT	\$\$\$\$	<0.0001		
				4-OHT versus E2+4-OHT	ns	>0.9999		
				VEGFR2				
				DMSO versus E2	ns	0.0699	DMSO	6
				DMSO versus 4-OHT	****	<0.0001	E2	6
	YES	one-way ANOVA	Bonferroni's multiple	DMSO versus E2+4-OHT	****	<0.0001	4-OHT	6
			comparisons test	E2 versus 4-OHT	\$\$\$\$	<0.0001	E2+4-OHT	6
				E2 versus E2+4-OHT	\$\$\$\$	<0.0001		
				4-OHT versus E2+4-OHT		>0.9999		1
	,			SCUBE2		0	DUGG	
				DMSO versus E2	****	<0.0001	DMSO	6
				DMSO versus 4-OHT	•	0.0425	E2	6
	YES	one-way ANOVA	Bonferroni's multiple	DMSO versus E2+4-OHT	ns	>0.9999	4-OHT	6
		, .	comparisons test	E2 versus 4-OHI	\$\$\$\$	<0.0001	E2+4-0H1	6
				E2 versus E2+4-OHT	\$\$\$\$	<0.0001		-
	I			4-OHT versus E2+4-OHT	ns	0.6559		
			1	ANGP12		0.0001	BM00	-
			Bonferroni's multiple	DMSO Versus E2	****	<0.0001	DMSO	6
		one-way ANOVA		DMSO versus 4-0H1	****	<0.0001	E2	6
	YES			E2 versus 4 OHT	2222	>0.9999	4-0HT	6
			companisons test			<0.0001	E2+4-0H1	0
						0.0001		-
	ļ			4-0111 Versus E244-0111		0.0001	1	
				DMSO versus E2	****	<0.0001	DMSO	6
		one-way ANOVA		DMSO versus 4-OHT	****	<0.0001	E2	6
Figure 4G	1/50		Bonferroni's multiple	DMSO versus E2+4-OHT	****	<0.0001	4-OHT	6
-	YES		comparisons test	E2 versus 4-OHT	\$\$\$	0.0005	E2+4-OHT	6
				E2 versus E2+4-OHT	\$\$\$	0.0004		1
				4-OHT versus E2+4-OHT	ns	>0.9999		
				DLL1				
				DMSO versus E2	ns	>0.9999	DMSO	6
		one-way ANOVA		DMSO versus 4-OHT	****	<0.0001	E2	6
	YES		Bonferroni's multiple	DMSO versus E2+4-OHT	****	<0.0001	4-OHT	6
			comparisons test	E2 versus 4-OHT	\$\$\$\$	<0.0001	E2+4-OHT	6
				E2 versus E2+4-OHT	\$\$\$\$	<0.0001		
				4-OHT versus E2+4-OHT	ns	0.7021		
			1 1	NOTCH1				
				DMSO versus E2	ns	>0.9999	DMSO	6
			Ponforrozia zwił	DMSO versus 4-0H1	****	<0.0001	EZ 4 OUT	0
1	YES	one-way ANOVA	comparisons test			<0.0001	4-UHI	6
			compansons test		\$\$\$\$	<0.0001	CZ+4-UHI	0
					φφφφ	>0.9999		-
				HEYL	110			J
	- I			DMSQ versus F2	****	<0.0001	DMSO	6
1			1	DMSO versus 4-OHT	ns	>0.9999	E2	6
	VEO		Bonferroni's multiple	DMSO versus E2+4-OHT	ns	<0.7732	4-OHT	6
	YES	one-way ANOVA	comparisons test	E2 versus 4-OHT	\$\$\$\$	<0.0001	E2+4-OHT	6
				E2 versus E2+4-OHT	\$\$\$\$	<0.0001		
				4-OHT versus E2+4-OHT	ns	>0.9999		1
				HEY2		•		
				DMSO versus E2	**	0.0027	DMSO	6
				DMSO versus 4-OHT	****	< 0.0001	E2	6
	YES	ODE-WOV ANOV/A	Bonferroni's multiple	DMSO versus E2+4-OHT	****	<0.0001	4-OHT	6
	120	one way ANOVA	comparisons test	E2 versus 4-OHT	\$\$\$\$	<0.0001	E2+4-OHT	6
				E2 versus E2+4-OHT	\$\$\$\$	<0.0001		
				4-OHT versus E2+4-OHT	ns	>0.9999		
				HEY2				
	I T			DMSO versus E2	**	0.0027	DMSO	6
				DMSO versus 4-OHT	****	<0.0001	E2	6
1	YES	one-way ANOVA	Bonferroni's multiple	DMSO versus E2+4-OHT	****	<0.0001	4-OHT	6
			comparisons test	E2 versus 4-OHT	\$\$\$\$	<0.0001	E2+4-OHT	6
1			1	E2 versus E2+4-OHT	\$\$\$\$	<0.0001		
				4-OHT versus E2+4-OHT	ns	>0.9999		1
1	<u> </u>			SOX7		0.0001	DUCC	-
				DMSO versus E2		<0.0001	DMSO	6
1			Bonforronia	DIVISO Versus 4-0H1	****	<0.0001	E2	6
1	YES	one-way ANOVA	comparisons tost		6444	<0.0001	4-UHI E2+4 OUT	0
1			compansons test		6666 9999	<0.0001	EZ+4-UHI	0
1					\$\$\$\$	>0.0001		
1			1 1	4-011 VE/SUS E2+4-001	115	- 0.0000		1

Piper Di Normaly Task Parkee me Company of the parkee me		Figure 5									
Piper St	Figure ID	Normality	Test	Post-hoc test	Comparison Summary		P-value	Sample size			
Part of the second of	3.0							Group	n		
Process AND(A) Restand(s) multiple emingenomises Disclosional bit (state) 4.00(1) 0000 (state) 4.00(1) 00000 (state) 4.00(1) 000000 00000 (state) 4.00(1)				-	PFKFB3						
YES are wey AUOUN Bodie more test and the appropriate test and the approprise test and the appropriate test appropriate test and the approp					DMSO versus E2		<0.0001	DMSO	6		
PTS one-say APC/A Descriptions use (originations use) DEC constructions (originations use) DEC constructions (originations use) Decords (originations use) Decords (originations use) <thdecords (originations="" th="" use)<=""></thdecords>				Bonferroni's multiple	DMSO versus 4-0HT	****	<0.0001		6		
Figure 2 Comparison of all and produced and		YES	one-way ANOVA		E2 versus 4 OHT	****	<0.0001	4-0HT	6		
Figure 5: Image: Second S				compansons test		\$\$\$\$ \$222	<0.0001	E2+4-0H1	0		
VES Ord-way AKD/A Defension and pro- comparison table comparison tab					4-OHT vorsus E2+4-OHT	9999 9999 9999	0.0684				
Piger Dr Order way AND/A Bordemon is notice DABO versus 6.247 ····································					4-0111 Versus E244-0111	115	0.0004		l		
VES and any ADD(A) Berteriorits multiple completion is multiple completion is multiple completion is multiple completion is multiple press Description is multiple bit result 24 CHT image: multiple bit result 24 CHT					DMSO versus E2	****	<0.0001	DMSO	6		
YEB one-mit ARXM Boldenois multiple one-mit ARXM DMSD sense 52-LOHT ····································			one-way ANOVA		DMSO versus 4-OHT	****	<0.0001	F2	6		
VES one way ANOVA Image: constrained bit in the second se				Bonferroni's multiple	DMSO versus E2+4-OHT	****	<0.0001	4-0HT	6		
Figure 50 Image: 10-10 (mode 12-4-0017) Image: 10-10 (mode 12-4-017) Image: 10-10 (mode 12-4-017) <td>YES</td> <td>comparisons test</td> <td>E2 versus 4-OHT</td> <td>\$\$\$\$</td> <td><0.0001</td> <td>E2+4-OHT</td> <td>6</td>		YES		comparisons test	E2 versus 4-OHT	\$\$\$\$	<0.0001	E2+4-OHT	6		
Fight 6					E2 versus E2+4-OHT	\$\$\$\$	<0.0001				
Figure 50 Contenting multiple (biothermit multiple (biothermit scholl) Contenting 22(-0)(1) Contenting 22(-0)(1) <thcontenting 22(-0)(1)<="" th=""> Contenting 22(-0)(1</thcontenting>					4-OHT versus E2+4-OHT	ns	>0.9999				
Figure Sci VES ane way ANDVA Bortemain mapped comparisons set comparisons set compari		НК2									
PES One-way ANDVA Borferon's multiple companions tast DMSD versus 24-04T ns 0.0500 E.P. 6. VES One-way ANDVA Borferon's multiple companions tast D.0500 VES 0.0500 E.P. 4-04T 6. VES One-way ANDVA Borferon's multiple companions tast D.0500 VES 0.0500 E.P. 4-04T 6. VES One-way ANDVA Borferon's multiple companions tast D.0500 versus 22+04T Time 0.0001 E.P. 4-04T 6. VES One-way ANDVA Borferon's multiple companions tast D.0500 versus 22+04T Time 0.0001 E.P. 4-04T E.P. 4-04T VES One-way ANDVA Borferon's multiple companions tast D.0500 versus 22+04T Time 0.0001 E.P. 4-04T E.P. 4-04T <t< td=""><td></td><td colspan="10">DMS0 versus E2 **** <0.000</td></t<>		DMS0 versus E2 **** <0.000									
YES one-way NOVA Bonformin multiple comparison test DASD ownary E2+4.ChT fits 0.1480 4-0hT 6 Figure 24 Comparison test E2 webs 42-0hT 55 0.0001 E24-42HT 6 Figure 24 Comparison test Comparison test Comparison test 0.0001 E24-42HT 0 VES one-way NOVA Bonferron's multiple comparison test Comparison test Comparison test 0.0001 E24 0 0.0001 E24 0 VES one-way NOVA Bonferron's multiple comparison test Comparison test Comparison test Comparison test 0.0001 E2 0 0 E2 0 0 E2 0 E2 0 E2 0 0 E2 0 E2 0 E2 0 E2 0 E2 E2 E2 E2 E2 E2 E2 E2 E2					DMSO versus 4-OHT	ns	0.5053	E2	6		
Figure 5 Line may ANOVA comparisons set Express 12-4017 SSS Express 12-4017 SSS Express 12-4017 Counce Express 12-4017 Figure 5 Counce Express 12-4017 SSS Express 12-4017 Counce Express 12-4017 SSS Express 12-4017 Counce Express 12-4017 <thcounce Express 12-4017 <thcounce Express 12-4017<!--</td--><td></td><td>VEC</td><td></td><td>Bonferroni's multiple</td><td>DMSO versus E2+4-OHT</td><td>ns</td><td>0.1450</td><td>4-OHT</td><td>6</td></thcounce </thcounce 		VEC		Bonferroni's multiple	DMSO versus E2+4-OHT	ns	0.1450	4-OHT	6		
Figure 5 Constrained by Constrated by Constrained by Constrated by Constrained by Cons		TES	one-way ANOVA	comparisons test	E2 versus 4-OHT	\$\$\$	0.0005	E2+4-OHT	6		
Figure 5 Image: Control of the second state of					E2 versus E2+4-OHT	\$\$	0.0021				
YES one-way ANOVA Device or is multiple comparison test comparison te					4-OHT versus E2+4-OHT	ns	>0.9999				
Figure 50 Part and particular set in training the comparison set in training traning training training traning training training t					ALDH3B1						
Figures one-way AND/A Bonterron's multiple comparisons test comparisons test comparisons test end OMSQ versus 24-0HT ······ ····· -0.0001 E2 / 6 -0.0001 E2 / 40H 6 -0.0001 VES 0 <td></td> <td></td> <td></td> <td></td> <td>DMSO versus E2</td> <td>****</td> <td><0.0001</td> <td>DMSO</td> <td>6</td>					DMSO versus E2	****	<0.0001	DMSO	6		
YES one-way ANDVA Bordemon's multiple comparisons test comparisons test per server ANDVA Bordemon's multiple E2 warms 24-0HT SSS -0.0001 4-0HT 6 Figure 50					DMSO versus 4-OHT	****	<0.0001	E2	6		
Figure 50 Constrained and the second se		VES		Bonferroni's multiple	DMSO versus E2+4-OHT	****	<0.0001	4-OHT	6		
Figure SC Image: Control in the state of th		TES	one-way ANOVA	comparisons test	E2 versus 4-OHT	\$\$\$\$	<0.0001	E2+4-OHT	6		
Figure SC					E2 versus E2+4-OHT	\$\$\$\$	<0.0001				
Figure SC DMSO versue E2 ···································					4-OHT versus E2+4-OHT	ns	>0.9999				
Figure 50 VES one-way ANOVA Destremon is unlique comparisons test ED Warsus 4-0HT					PDK4						
YES one-way ANOVA Borderon's multiple comparisons test DMSO versus 42+0-HT ······ -0.0001 E2+0-HT 6 Figure SC YES one-way ANOVA Borderon's multiple comparisons test -0.0001 E2+0-HT 6 -					DMSO versus E2	****	<0.0001	DMSO	6		
YES one-way ANOVA Bonferron's multiple comparison steat DMSO versus 24-0HT ······ -4.001 24-0HT 6 Figure SC YES one-way ANOVA Bonferron's multiple comparison steat DMSO versus 24-0HT me 0.0001 E24-0HT ne 0.01227 ne YES one-way ANOVA Bonferron's multiple comparison steat DMSO versus 42-0HT me 0.0001 E24-0HT ne 0.0001 E24-0HT					DMSO versus 4-OHT	****	<0.0001	E2	6		
Figure SC One-way ANOVA Comparison test comparison stest E2 versus E2+4-OHT E2 versus E2+4-OHT SSSS c0.0001		VES		Bonferroni's multiple	DMSO versus E2+4-OHT	****	<0.0001	4-OHT	6		
Figure SC E2 varue E2+4-OHT SSSS		120	one way Altowa	comparisons test	E2 versus 4-OHT	\$\$\$\$	<0.0001	E2+4-OHT	6		
Figure SC Image: constraint of the second seco					E2 versus E2+4-OHT	\$\$\$\$	<0.0001				
Figure SC WES 0.00-way ANOVA Marcine SC 1000 multiple Comparison stet Colspan="2">Colspan="2">Colspan="2">Colspan="2">Colspan="2">Colspan="2">Colspan="2">Colspan="2">Colspan="2">Colspan="2">Colspan="2" Figure SC Cone-way ANOVA Bonterron's multiple Comparison stet Colspan="2">Colspan="2">Colspan="2">Colspan="2" VES Cone-way ANOVA Bonterron's multiple Comparison stet Colspan="2" Colspan="2" VES Cone-way ANOVA Bonterron's multiple Comparison stet Colspan="2" Colspan="2" VES Cone-way ANOVA Bonterron's multiple Comparison stet Colspan="2" Colspan="2" Colspan="2" VES One-way ANOVA Bonterron's multiple Comparison stet Colspan="2" Colspan="2" VES One-way ANOVA Bonterron's multiple Comparison stet Colspan="2" Colspan="2" Colspan="2" VES One-way ANOVA Bonterron's multiple Comparison stet Colspan="2" Colspan="2" Colspan="2" VES <t< td=""><td></td><td></td><td>4-OHT versus E2+4-OHT</td><td>ns</td><td>0.1927</td><td></td><td></td></t<>					4-OHT versus E2+4-OHT	ns	0.1927				
Figure SC YES Ane-way ANOVA Bonterron's multiple comparisons test expansions DMSO versus E2 (+4-OHT) ms -0.0001 (-0.0001) DMSO (-0.0001) (-0.0001) E2+4-OHT (-0.0001) Comparisons test (-0.0001) Comparison test (-0.0001) Comparison test (-0.0001) Comparison test (-0.0001) Comparison test (-0.0001) Comparison test (-0.0001) Comparison test (-0.0001)		MPC1									
Figure SC YES one-way ANOVA Enderon's multiple comparisons test comparisons test express 4-0HT ns >0.9999 E2 6 VES one-way ANOVA Enderon's multiple comparisons test express 4-0HT 0.5537 4-0HT 6 VES one-way ANOVA Express 4-0HT 0.5537 4-0HT 6 VES one-way ANOVA Express 4-0HT ns 0.0224 0 VES one-way ANOVA Benferon's multiple comparisons test DMSO versus 22+4-0HT ns 0.0001 E2 0 VES one-way ANOVA Benferon's multiple comparisons test DMSO versus 22+4-0HT 0.001 E2 0 0 6 0			one-way ANOVA		DMSO versus E2	****	<0.0001	DMSO	6		
Figure SC YES one-way ANOVA Bonferron's multiple comparisons test E2 versus 62-4-OHT ns 0.1537 4-OHT 6 VES one-way ANOVA Bonferron's multiple comparisons test E2 versus 62-4-OHT SSSS <0.0001					DMSO versus 4-OHT	ns	>0.9999	E2	6		
Har My More comparison test E2 versus E2+4-OHT SSSS -0.0001 E2-44-OHT 6 YES one-way ANOVA Bonferron's multiple comparison test DMSO versus E2	Figure 5C	YES		Bonferroni's multiple	DMSO versus E2+4-OHT	ns	0.1537	4-OHT	6		
E2 Description E2+4-OHT SSS -0.0001 M Interval and the example of the examp				comparisons test	E2 versus 4-OHT	\$\$\$\$	<0.0001	E2+4-OHT	6		
VES 0.2224 0.2224 0.2224 YES 0ne-way ANOVA Bonferron's multiple comparisons test DMSO versus E2 **** -0.0001 DMSO 6 DMSO versus E2 **** -0.0001 DMSO 6 DMSO versus E2+4-OHT **** -0.0001 E2+4-OHT 6 DMSO versus E2+4-OHT ms -0.0001 2+4-OHT 6 E2 versus E2+4-OHT ms -0.0001 DMSO 6 DMSO versus E2+4-OHT ms -0.0001 E2+4-OHT 6 DMSO versus E2+4-OHT ms -0.0001 DMSO 6 DMSO versus E2+4-OHT ms -0.00120 4-OHT 6 DMSO versus E2+4-OHT *** -0.0010 DMSO 6 DMSO versus E2+4-OHT *** -0.0011 DMSO 6 DMSO versus E2+4-OHT *** -0.0011 DMSO 6 DMSO versus E2+4-OHT ms -0.0001 DMSO 6 DMSO versus E2+4-OHT ms -0.0001 <					E2 versus E2+4-OHT	\$\$\$\$	<0.0001				
VES ONSO versus E2 **** ONSO versus E2+4-OHT **** **** ONSO versus E2+4-OHT **** ONSO versus E2+4-OHT **** **** ONSO versus E2+4-OHT ***** ***** **** ****** ***** ****** ****** ***********************************					4-OHT versus E2+4-OHT	ns	0.2224				
YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 62/L DMSO versus 62-4 CHT ················ <d.0001< th=""> DMSO 6 E 6 DMSO versus 62-4 CHT YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 62-4 CHT ····································</d.0001<>					AACS		1				
YES one-way ANOVA DMSO versus E2+4-OHT imm <td></td> <td></td> <td></td> <td></td> <td>DMSO versus E2</td> <td></td> <td><0.0001</td> <td>DMSO</td> <td>6</td>					DMSO versus E2		<0.0001	DMSO	6		
YES one-way ANOVA Bonterron's multiple comparisons test comparisons test expanses of the second expanses of the second expanse of the second			one-way ANOVA		DMSO versus 4-OHI		<0.0001	E2	6		
VES comparisons test E2 versus E2+4-OHT SSSS <0.0001 E2+4-OH1 6 VES 0ne-way ANOVA Bonferron's multiple comparisons test DMSO versus E2+4-OHT ns >0.0999 0 YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus E2+4-OHT **** <0.0011		YES		Bonferroni's multiple	DMSO versus E2+4-OH1		<0.0001	4-0H1	6		
LE2 Versus E24-40HT SSSS <0.0001 Le3 VES one-way ANOVA Bonferron's multiple DMS0 versus E2 **** <0.0001				comparisons test	E2 versus 4-OHT	\$\$\$\$	<0.0001	E2+4-0H1	6		
VES one-way ANOVA Bonterron's multiple comparisons test DMSO versus E2 DMSO versus E2+4-OHT **** A0.999 MSO 6 YES one-way ANOVA Bonterron's multiple comparisons test DMSO versus E2+4-OHT **** <0.0001					E2 versus E2+4-OHI	\$\$\$\$	<0.0001				
VES One-way ANOVA DMSO versus E2 **** ONGO COLSPAN ONGO <th colspan="2</td> <td></td> <td></td> <td></td> <td></td> <td>4-OHT versus E2+4-OHT</td> <td>ns</td> <td>>0.9999</td> <td></td> <td></td>					4-OHT versus E2+4-OHT	ns	>0.9999				
YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 22.4 -OHT ** 0.0020 4-OHT 6 YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 22.4 -OHT * 0.0120 4-OHT 6 YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 22.4 -OHT rss >0.0999 0 YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 52 ***** <0.0001				-	ALSSI	****	0.0004	DMCO	6		
YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus E2+4-OHT * 0.0038 E2 0 YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus E2+4-OHT \$					DMSO versus 4 OUT	**	<0.0001	DIVISO	6		
YES one-way ANOVA DOMENDIAL SITURDING comparisons test Discoversus E2+4-OHT SSSS <0.0001 E2+4-OHT 6 E2 versus E2+4-OHT SSSS <0.0001				Bonforronia multi-l-			0.0038	EZ 4-OUT	6		
VES Comparison dest E2 versus 2+4-OHT 33333 224+OHT 5 YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus E2+4-OHT ns >0.0999 0		YES	one-way ANOVA	comparisons tost		2222	<0.0120	4-UHI	6		
VES One-way ANOVA Bonferron's multiple comparisons test DMSO versus 24-4-OHT DMSO versus 4-0HT 0.0001 00000000000000000000000000000000				compansons test	E2 Versus 4-OHT	\$\$\$\$	<0.0001	E2+4-UH1	0		
VES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 4-0HT ins A0.0001 DMSO 6 YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 4-0HT ***** <0.0001						3333	<0.0001				
YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 4-0HT **** <0.0001 DMSO 6 VES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 4-0HT **** <0.0001					4-OHT Versus E2+4-OHT	115	, 0.0000		l		
YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 24-0HT **** <0.0001 E2 6 VES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 22.4-0HT **** <0.0001		-			DMSO versus E2	****	<0.0001	DMSO	6		
YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 24-4-OHT **** <0.0001 4-OHT 6 E2 versus 4-OHT \$					DIVISO Versus 2 OHT	****	-0.0001	E2	6		
YES one-way ANOVA Domentity instance Differentity instance Differentity instance Differentity instance Differentity instance Comparison test E2 versus 4-0HT SSSS <0.0001 E2+4-0HT 6 VES one-way ANOVA E2 versus 4-0HT SSSS <0.0001				Bonforroni's multiple	DMSO versus E2+4-0HT	****	<0.0001		6		
VES One-way ANOVA Bonferron's multiple comparisons test DMSO versus E2+4-OHT 00000 00.0001 DMSO 6 YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus E2+4-OHT ns >0.09999 4-OHT 6 YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus E2+4-OHT ns >0.08814 E2 6 VES one-way ANOVA Bonferron's multiple comparisons test DMSO versus E2+4-OHT ns >0.09999 4-OHT 6 VES one-way ANOVA Bonferron's multiple comparisons test DMSO versus E2+4-OHT ns >0.09999 4-OHT 6 VES one-way ANOVA Bonferron's multiple comparisons test DMSO versus E2+4-OHT ns >0.09999 4-OHT 6 VES one-way ANOVA Bonferron's multiple comparisons test DMSO versus E2+4-OHT ns >0.0001 DMSO 6 DMSO versus E2+4-OHT ms <0.0001		YES	one-way ANOVA	comparisons test	E2 vorsus 4-OHT	2222	<0.0001	E2+4-0HT	6		
Understand Underst				compansons test	E2 versus E2 4-0HT	0000 0000	<0.0001	2214 0111	0		
YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 22 DMSO versus 4:0HT **** <0.0001 DMSO 6 YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 4:0HT ns >0.0814 E2 6 VES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 4:0HT ns >0.09999 4-OHT 6 VES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 2:4-0HT ms >0.09999 4-OHT 6 VES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 2:4-0HT ns >0.09999 4 VES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 4:0HT ms <0.0001					4-OHT vorsus E2+4-OHT	addad De	>0.9999				
YES One-way ANOVA DMSO versus 4-0HT DMSO versus 4-0HT ns 0.6814 E2 6 DMSO versus 4-0HT ns 0.6814 E2 6 DMSO versus 4-0HT ns 0.6814 E2 6 DMSO versus 4-0HT ns >0.9999 4-0HT 6 E2 versus 24-0HT \$					GLUT1	10			-		
YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 4-OHT ns 0.6814 E2 6 YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus 4-OHT ns >0.9999 4-OHT 6 YES one-way ANOVA E2 versus 4-OHT SSSS <0.0001					DMSO versus E2	****	<0.0001	DMSO	6		
YES one-way ANOVA Bonferron's multiple comparisons test DMSO versus E2+4-OHT ns >0.9999 4-OHT 6 VES one-way ANOVA Bonferron's multiple comparisons test DMSO versus E2+4-OHT SSSS <0.0001					DMSO versus 4-OHT	ns	0.6814	F2	6		
YES one-way ANOVA Someway ANOVA				Bonferroni's multiple	DMSO versus E2+4-OHT	ns	>0.9999	4-0HT	6		
E2 versus E2+4-OHT \$\$\$\$\$ <0.0001 Image: Constraint of the system of		YES	one-way ANOVA	comparisons test	E2 versus 4-OHT	\$\$\$\$	<0.0001	E2+4-OHT	6		
Image: Control of the state of the	1				E2 versus E2+4-OHT	\$\$\$\$	<0,0001		<u> </u>		
Bonferron's multiple DMSO versus E2 **** <0.0001 DMSO 6 DMSO versus 4-0HT **** <0.0001					4-OHT versus F2+4-OHT	ns	>0.9999				
YES one-way ANOVA DMSO versus E2 DMSO versus 24-OHT **** **** <0.0001 DMSO 6 E2 6 6 DMSO versus 24-OHT **** <0.0001					GLUT4						
YES One-way ANOVA Deferron's multiple comparisons test DMSO versus 4-OHT **** <0.0001 E2 6 E2 versus 4-OHT **** <0.0001					DMSO versus E2	****	<0.0001	DMSO	6		
YES One-way ANOVA Bonferron's multiple comparisons test DMSO versus E2+4-OHT **** <0.0001 4-OHT 6 E2 versus 4-OHT ns >0.9999 E2+4-OHT 6 E2 versus 4-OHT \$\$ 0.0051 4 4-OHT versus E2+4-OHT \$\$ 0.0051 4					DMSO versus 4-OHT	****	<0,0001	F2	6		
YES one-way ANOVA Comparisons test E2 versus 4-0HT ns >0.9999 E2+4-0HT 6 4-0HT versus E2+4-0HT \$\$ 0.0051 4 4 4 4 4 4 4 4 5 0.0010 4 4 5 0.0010 4 6			S one-way ANOVA	ANOVA Bonferroni's multiple comparisons test	DMSO versus E2+4-OHT	****	<0.0001	4-0HT	6		
E2 versus E2+4-OHT \$\$ 0.0051 4-OHT versus E2+4-OHT ††† 0.0010		YES			E2 versus 4-OHT	ns	>0.9999	E2+4-OHT	6		
4-OHT versus E2+4-OHT					E2 versus E2+4-OHT	\$\$	0.0051	1			
					4-OHT versus E2+4-OHT	<u>+++</u>	0.0010				

	Figure 6								
Figure ID	Normality	Test	Post-hoc test	Comparison Summary		P-value	Sample	size	
	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,				,		Group	n	
				NR2F6			-		
				DMSO versus E2	****	<0.0001	DMSO	6	
				DMSO versus 4-OHT		<0.0001	E2	6	
	YES	one-way ANOVA	Bonferroni's multiple	DMSO versus E2+4-OHT		<0.0001	4-OHT	6	
			comparisons test	E2 versus 4-OHT	\$\$\$\$	<0.0001	E2+4-OHT	6	
				E2 versus E2+4-OHT	\$\$\$\$	<0.0001			
				4-OHT versus E2+4-OHT	ns	>0.9999			
				-					
				DMSO versus E2	**	0.0046	DMSO	6	
				DMSO versus 4-OHT	****	<0.0001	E2	6	
Figure 6D	YES	one-way ANOVA	Bonferroni's multiple	DMSO versus E2+4-OHT	***	<0.0001	4-OHT	6	
			comparisons test	E2 versus 4-OHT	\$	<0.0001	E2+4-OHT	6	
				E2 versus E2+4-OHT	ns	<0.0001			
				4-OHT versus E2+4-OHT	ns	>0.9999			
				LTF				-	
				DMSO versus E2	****	<0.0001	DMSO	6	
				DMSO versus 4-OHT	****	<0.0001	E2	6	
	VES		Bonferroni's multiple	DMSO versus E2+4-OHT	****	<0.0001	4-OHT	6	
	120	one way Artovia	comparisons test	E2 versus 4-OHT	\$\$\$\$	<0.0001	E2+4-OHT	6	
				E2 versus E2+4-OHT	\$\$\$\$	<0.0001			
				4-OHT versus E2+4-OHT	ns	>0.9999			
				KLF2					
		one-way ANOVA		DMSO versus E2	****	<0.0001	DMSO	6	
				DMSO versus 4-OHT	****	<0.0001	E2	6	
	VEC		VA Bonferroni's multiple comparisons test	DMSO versus E2+4-OHT	****	<0.0001	4-OHT	6	
	TES			E2 versus 4-OHT	\$\$	0.0041	E2+4-OHT	6	
				E2 versus E2+4-OHT	\$	0.0323			
				4-OHT versus E2+4-OHT	ns	>0.9999			
	KLF13								
	YES	one-way ANOVA	Bonferroni's multiple comparisons test	DMSO versus E2	****	<0.0001	DMSO	6	
				DMSO versus 4-OHT	****	<0.0001	E2	6	
				DMSO versus E2+4-OHT	****	<0.0001	4-OHT	6	
				E2 versus 4-OHT	\$\$\$\$	<0.0001	E2+4-OHT	6	
				E2 versus E2+4-OHT	\$\$\$\$	<0.0001			
				4-OHT versus E2+4-OHT	ns	0.8496			
				EGR1					
		one-way ANOVA		DMSO versus E2	****	<0.0001	DMSO	6	
				DMSO versus 4-OHT	****	<0.0001	E2	6	
	VEC		Bonferroni's multiple	DMSO versus E2+4-OHT	****	<0.0001	4-OHT	6	
	123		comparisons test	E2 versus 4-OHT	\$\$\$\$	<0.0001	E2+4-OHT	6	
				E2 versus E2+4-OHT	\$\$\$\$	<0.0001			
Figure 6H				4-OHT versus E2+4-OHT	ns	0.5786			
Figure on				FOXC1					
				DMSO versus E2	**	0.0020	DMSO	6	
				DMSO versus 4-OHT	ns	>0.9999	E2	6	
	NO		Dunn's multiple	DMSO versus E2+4-OHT	ns	>0.9999	4-OHT	6	
	NO	Kruskai-wallis	comparisons test	E2 versus 4-OHT	ns	0.0682	E2+4-OHT	6	
				E2 versus E2+4-OHT	\$	0.0423			
				4-OHT versus E2+4-OHT	ns	>0.9999			
				HOXB6					
				DMSO versus E2	****	<0.0001	DMSO	6	
				DMSO versus 4-OHT	****	<0.0001	E2	6	
	1/50		Bonferroni's multiple	DMSO versus E2+4-OHT	****	<0.0001	4-OHT	6	
	YES	one-way ANOVA	comparisons test	E2 versus 4-OHT	\$\$\$\$	<0.0001	E2+4-OHT	6	
				E2 versus E2+4-OHT	\$\$\$\$	<0.0001			
				4-OHT versus E2+4-OHT	ns	0.3984			
				HOXB7					
				DMSO versus E2	****	<0.0001	DMSO	6	
				DMSO versus 4-OHT	****	<0.0001	E2	6	
	1000		Bonferroni's multiple	DMSO versus E2+4-OHT	****	<0.0001	4-OHT	6	
	YES	one-way ANOVA	comparisons test	E2 versus 4-OHT	\$\$\$\$	< 0.0001	E2+4-OHT	6	
			companions test	E2 versus E2+4-OHT	\$\$\$\$	< 0.0001		-	
				4-OHT versus E2+4-OHT	ns	>0.9999			

Figure ID	Normality	Test	Post-hos tost	Comparison	Summary	P-value	Sample size			
	Normanty		FUSI-HUC LESI				Group	n		
	ESR1									
	NO) Kruskal-Wallis		hERaWT DMSO versus hERaWT E2	ns	0.8462	hERaWT DMSO	3		
				hERaWT DMSO versus hERaWT 4-OHT	ns	0.5366	hERaWT E2	3		
Figure S1A			Kruskal-Wallic Dunn's multiple	hERaWT DMSO versus hERaWT E2+4-OHT	•	0.0194	hERαWT 4-OHT	3		
			comparisons test	hERaWT E2 versus hERaWT 4-OHT	ns	>0.9999	hERaWT E2+4-OHT	3		
				hERaWT E2 versus hERaWT E2+4-OHT	ns	0.8462				
				hERaWT 4-OHT versus hERaWT E2+4-OHT	ns	>0.9999				

Appendix S2										
Figure ID	Normality	Test	Post-hoc test	Comparison Summary		P-value	Sample	size		
	,				,		Group hERa	n		
			- 1	VEGFA	-		1			
				DMSO versus E2	•	0.0206	DMSO	6		
				DMSO versus 4-OHT	ns	>0.9999	E2	6		
	YES	one-way ANOVA	Bonferroni's multiple	DMSO versus E2+4-OHT	ns	>0.9999	4-OHT	6		
		one way ArtovA	comparisons test	E2 versus 4-OHT	\$\$\$	0.0009	E2+4-OHT	6		
				E2 versus E2+4-OHT	\$	0.0451		L		
				4-OHT versus E2+4-OHT	ns	>0.9999				
				VEGFR2			L			
				DMSO versus E2	ns	0.6518	DMSO	6		
				DMSO versus 4-OHT	****	<0.0001	E2	6		
	YES	one-way ANOVA	Bonferroni's multiple	DMSO versus E2+4-OHT	*	<0.0001	4-OHT	6		
			comparisons test	E2 versus 4-OHT	\$\$	0.0016	E2+4-OHT	6		
				E2 versus E2+4-OHT	\$\$	0.0043				
				4-OHT versus E2+4-OHT	ns	>0.9999]		
				DLL4			I.			
				DMSO versus E2	****	<0.0001	DMSO	6		
				DMSO versus 4-OHT	****	<0.0001	E2	6		
	YES	one-way ANOVA	Bonferroni's multiple	DMSO versus E2+4-OHT	****	<0.0001	4-OHT	6		
			comparisons test	E2 versus 4-OHT	ns	>0.9999	E2+4-OHT	6		
				E2 versus E2+4-OHT	ns	>0.9999		L		
				4-OHT versus E2+4-OHT	ns	>0.9999		1		
	HEY2									
	YES	one-way ANOVA	Bonferroni's multiple comparisons test	DMSO versus E2	**	0.0019	DMSO	6		
				DMSO versus 4-OHT	****	<0.0001	E2	6		
				DMSO versus E2+4-OHT	****	<0.0001	4-OHT	6		
				E2 versus 4-OHT	\$\$\$\$	<0.0001	E2+4-OHT	6		
		I.		E2 versus E2+4-OHT	\$\$\$\$	< 0.0001		L		
Figure S2				4-OHT versus E2+4-OHT	ns	>0.9999				
	PFKFB3									
		one-way ANOVA		DMSO versus E2	**	0.0065	DMSO	6		
				DMSO versus 4-OHT	ns	>0.9999	E2	6		
	YES		Bonferroni's multiple	DMSO versus E2+4-OHT	ns	>0.9999	4-OHT	6		
			comparisons test	E2 versus 4-OHT	\$\$	0.0019	E2+4-OHT	6		
				E2 versus E2+4-OHT	\$\$	0.0047		L		
				4-OHT versus E2+4-OHT	ns	>0.9999		1		
	GLUTT									
		one-way ANOVA		DMSO versus E2	****	<0.0001	DMSO	6		
				DMSO versus 4-OHT	****	<0.0001	E2	6		
	YES		Bonferroni's multiple	DMSO versus E2+4-OHT	****	<0.0001	4-OHT	6		
			comparisons test	E2 versus 4-OHT	ns	>0.9999	E2+4-OHT	6		
				E2 versus E2+4-OHT	ns	>0.9999		L		
	4-OHT versus E2+4-OHT ns >0.9999									
				PDK4						
				DMSO versus E2	****	<0.0001	DMSO	6		
				DMSO versus 4-OHT	ns	>0.9999	E2	6		
	YES	one-way ANOVA	Bonferroni's multiple	DMSO versus E2+4-OHT	ns	0.0595	4-OHT	6		
		one-way ANOVA	comparisons test	E2 versus 4-OHT	\$\$\$\$	<0.0001	E2+4-OHT	6		
				E2 versus E2+4-OHT	\$\$\$\$	<0.0001		L		
l I				4-OHT versus E2+4-OHT	ns	0.5497				
	ļ,		1	MPC1						
				DMSO versus E2	****	<0.0001	DMSO	6		
				DMSO versus 4-OHT	ns	>0.9999	E2	6		
	YES	one-way ANOVA	Bonferroni's multiple comparisons test	DMSO versus E2+4-OHT	ns	>0.9999	4-OHT	6		
	120			E2 versus 4-OHT	\$\$\$\$	<0.0001	E2+4-OHT	6		
				E2 versus E2+4-OHT	\$\$\$\$	<0.0001		L		
				4-OHT versus E2+4-OHT	ns	>0.9999				

	Appendix S3										
Figure ID	Normality	Test	Post-hoc test	ost-hoc test Comparison Summary P-value		P-value	Sample size	ė	Sample size	ف	
0.0	,						Group NT	n	Group hERa	n	
				N	IR2F6		- i-				
				P-interaction between Genotype and Treatment	<0.0001	****	DMSO	5	DMSO	6	
				P Genotype	<0.0001	****	E2	6	E2	6	
	VES		Bonferroni's multiple	P Treatment	<0.0001	****	4-OHT	5	4-OHT	6	
	125	ino-way Artoria	comparisons test				E2+4-OHT	6	E2+4-OHT	6	
	ETS2										
				P-interaction between Genotype and Treatment	0.0137	+	DMSO	5	DMSO	6	
				P Genotype	0.0223	+	E2	6	E2	6	
	1/50		Bonferroni's multiple	P Treatment	<0.0001	****	4-OHT	5	4-OHT	6	
	YES	two-way ANOVA	comparisons test				E2+4-OHT	6	E2+4-OHT	6	
			_							+	
			1 1	si	MAD1	1					
		two-way ANOVA	Bonferroni's multiple comparisons test	P-interaction between Genotype and Treatment	0.2305	ns	DMSO	5	DMSO	6	
				P Genotine	0.3293	ns	F2	6	F2	6	
	YES			P Treatment	<0.0001	****	4-0HT	5	4-OHT	6	
				/ Heathent	40.0001		E2+4-OHT	6	E2+4-OHT	6	
							E2++OIII	-	E2++OITI		
								-			
Figure S3				N	R2F2	1			·	4	
				R interaction between Country and Tractment	0.1561		DMSO	5	DMSO	6	
		two-way ANOVA	-	P-Interaction between Genotype and Treatment	0.1301	115	DIVISO		DIVIGO	0	
			Bonforroni'o multiplo	P Genotype	<0.0001	**	4 OUT	6	EZ 4 OUT	6	
	YES		Bonierroni s muluple	P Treatment	0.0039		4-UH1	5	4-011	0	
			companisons test				E2+4-UH1	0	E2+4-0H1	0	
									l	1	
			l la	SI	WAD6	1	1				
				P-interaction between Genotype and Treatment	0.6219	ns	DMSO	5	DMSO	6	
				P Genotype	<0.0001		E2	6	E2	6	
	YES	two-way ANOVA	Bonferroni's multiple	P Treatment	<0.0001	****	4-OHT	5	4-OHT	6	
			comparisons test				E2+4-OHT	6	E2+4-OHT	6	
				F	OXC1					-	
				P-interaction between Genotype and Treatment	<0.0001	****	DMSO	5	DMSO	6	
				P Genotype	<0.0001	****	E2	6	E2	6	
	YES	two-way ANOVA	Bonferroni's multiple	P Treatment	<0.0001	****	4-OHT	5	4-OHT	6	
		the may ANOTA	comparisons test				E2+4-OHT	6	E2+4-OHT	6	