

Supplementary Materials for
**Mitochondrial-targeted antioxidant attenuates preeclampsia-like phenotypes
induced by syncytiotrophoblast-specific Gαq signaling**

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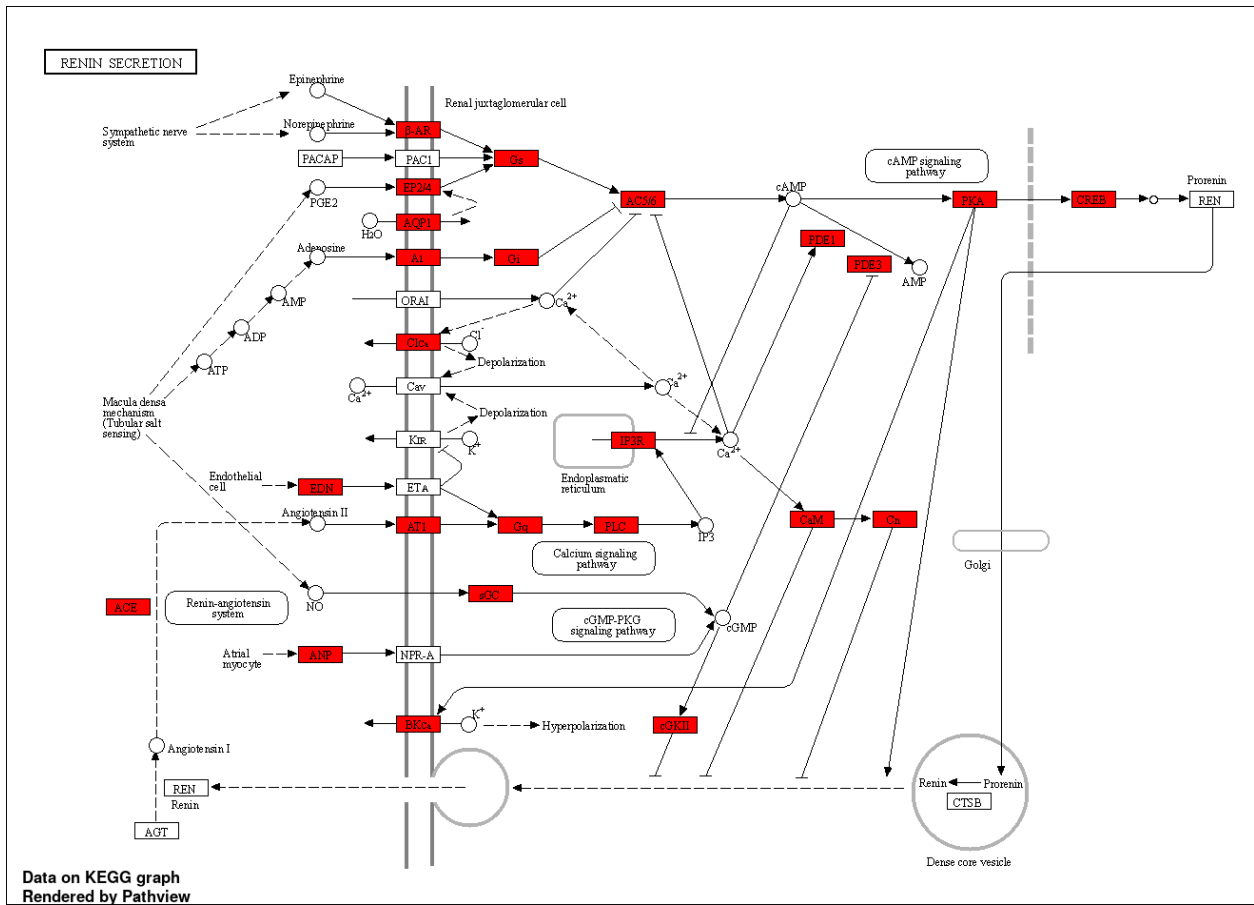


Fig. S1. KEGG pathway analysis for renin secretion within a human placental microarray dataset (GSE75010) using ShinyGO 0.77. Red indicates enrichment within the differentially expressed gene set in preterm preeclampsia (n=49) vs. preterm control (n=35).

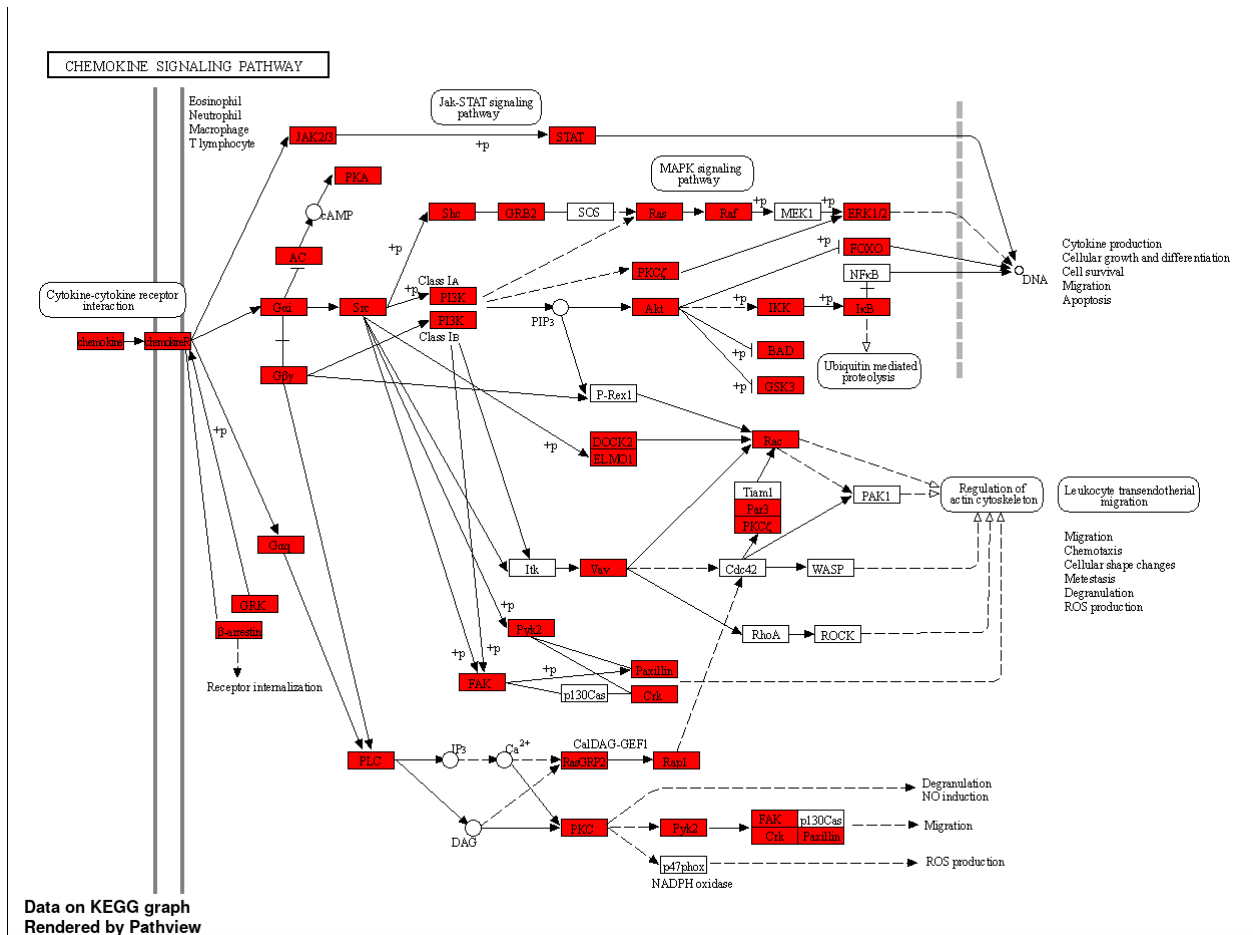


Fig. S2. KEGG pathway analysis for chemokine signaling within a human placental microarray dataset (GSE75010) using ShinyGO 0.77. Red indicates enrichment within the differentially expressed gene set in preterm preeclampsia (n=49) vs. preterm control (n=35).

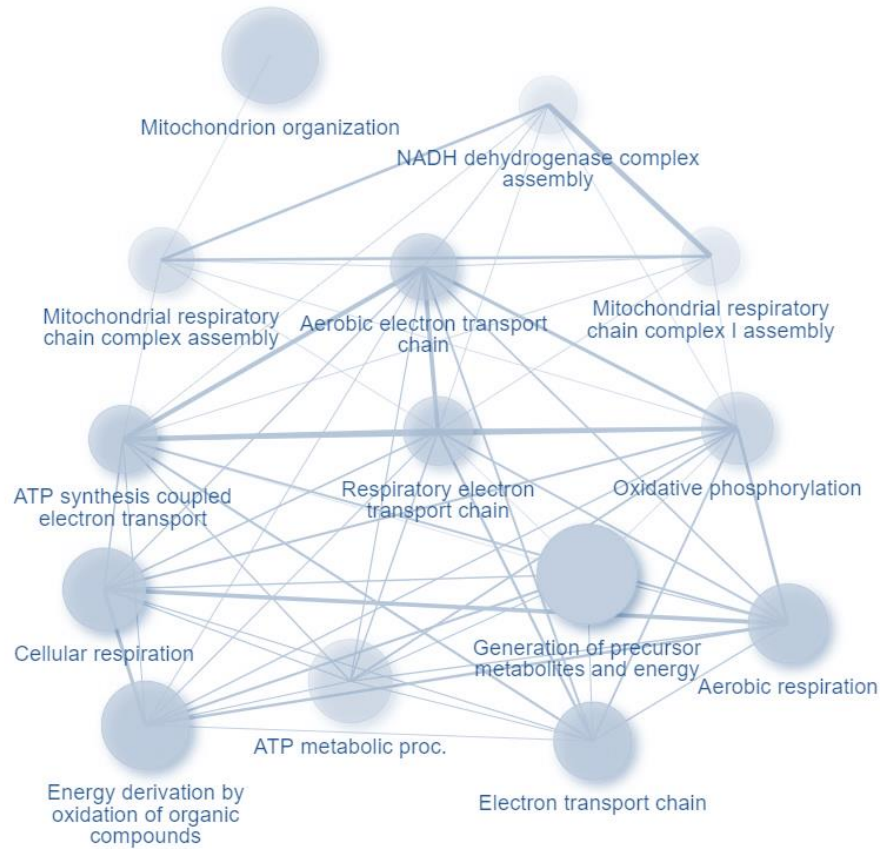


Fig. S3.
Network analysis among downregulated genes during preterm preeclampsia (n=49) vs. preterm control (n=35) within a human placental microarray dataset (GSE75010).

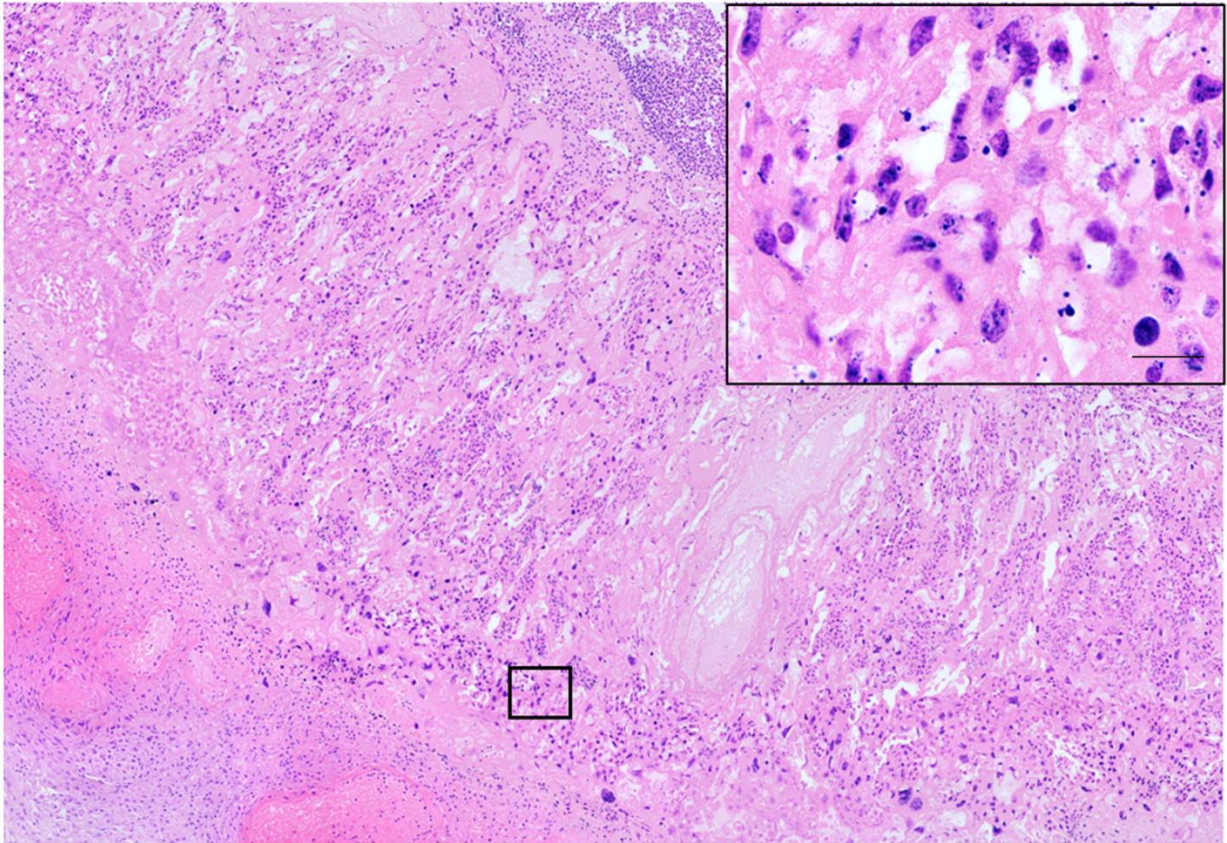


Fig S4.

Hematoxylin and eosin-stained placenta tissue from a CNO-injected *hM3Dq*^{F/F} dam x *Actb-Cre*^{+/+} sire pregnancy at GD 14.5. Scale bar: 25 μ m.

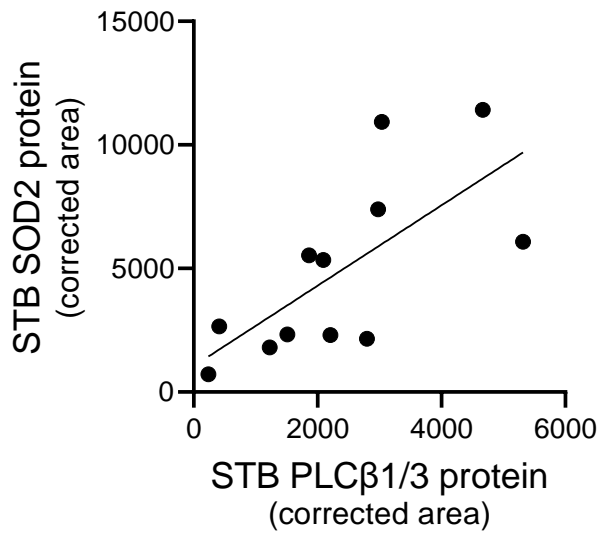


Fig. S5.

Correlation between PLCβ1/PLCβ3 and SOD2 protein expression in laser capture microdissected human syncytiotrophoblast cells; STB, syncytiotrophoblast.

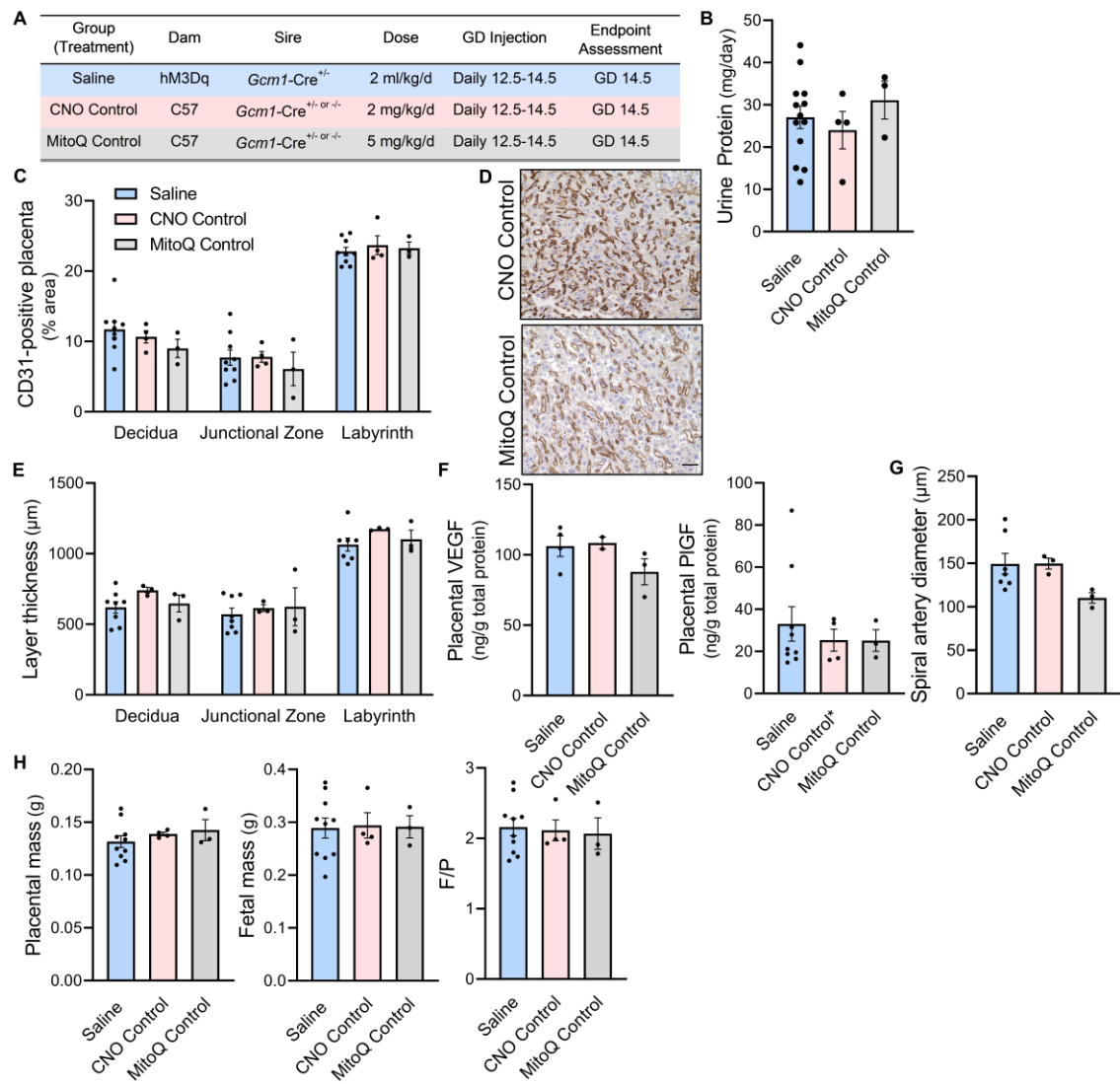


Fig. S6.

Independent effects of CNO and MitoQ administration during pregnancy at GD 14.5. (A) Details of control pregnancy cohorts. (B) 24-hour maternal urine protein excretion. (C) Total vascularization within each primary layer of the mouse placenta, evaluated by CD31 immunohistochemistry. (D) Representative labyrinth image of DAB immunostain for CD31. Scale bars: 50µm. (E) Thickness of each placental layer. (F) Placental VEGF and PlGF protein content. (G) Average luminal diameter of decidual spiral arteries. (H) Placental mass, fetal mass, and fetal mass/placental mass.

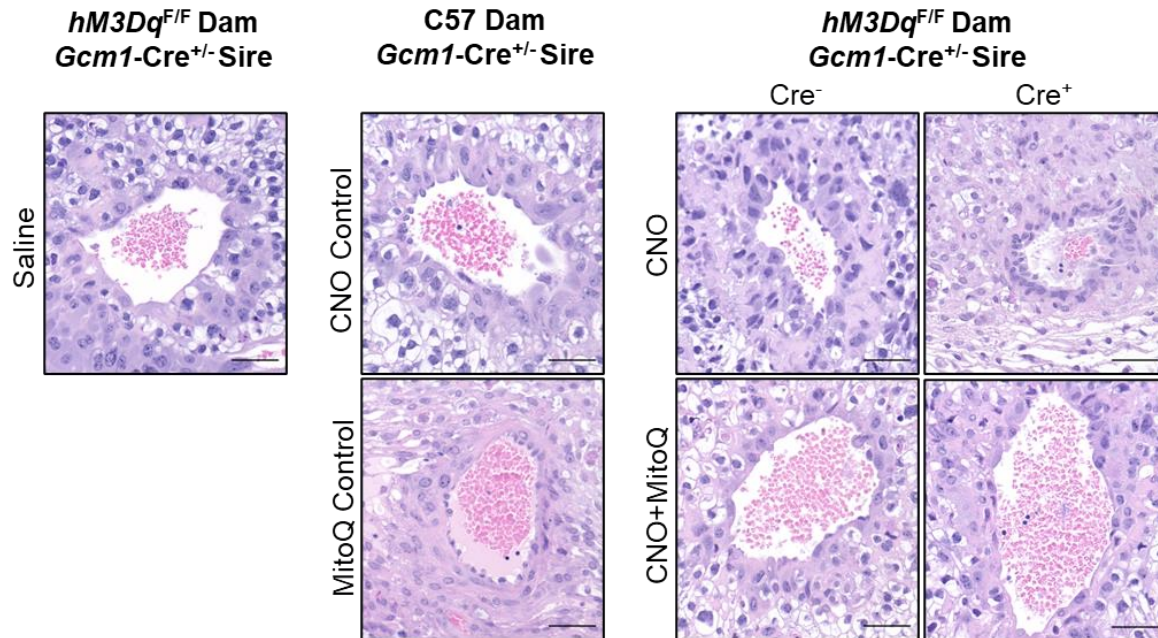


Fig. S7.
Representative spiral artery images within hematoxylin and eosin-stained placenta at GD 14.5. Scale bars: 50 μ m.

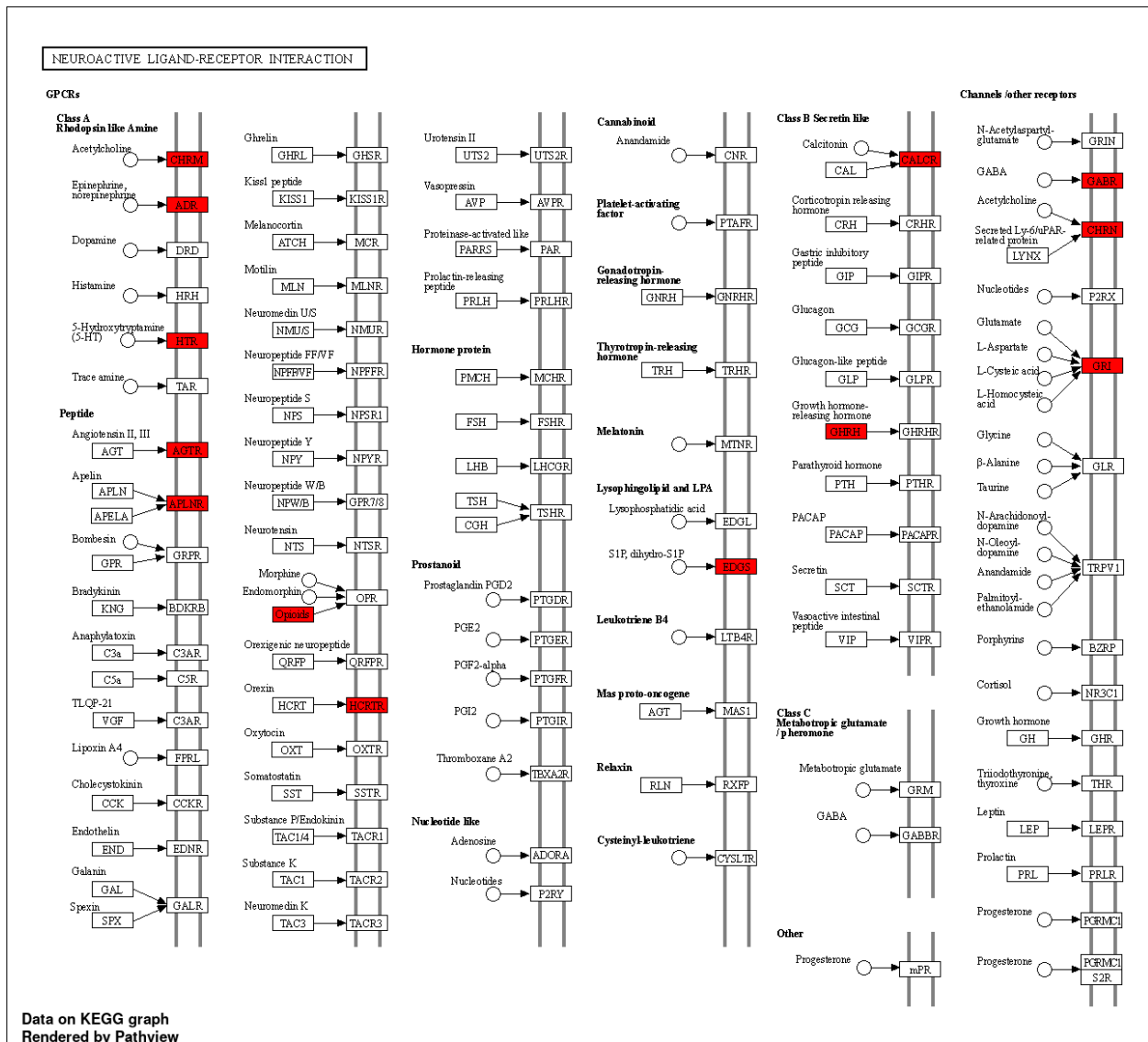


Fig. S8. KEGG pathway analysis for neuroactive ligand-receptor interactions (ShinyGO 0.77) within the upregulated gene set in CNO Cre⁺ placenta vs. controls (Saline, CNO Cre⁻) determined by bulk RNA-sequencing (n=6 per group, *hM3Dq*^{F/F} dam x *Gcm1-Cre*^{+/-} sire, GD 14.5). Red indicates enrichment.

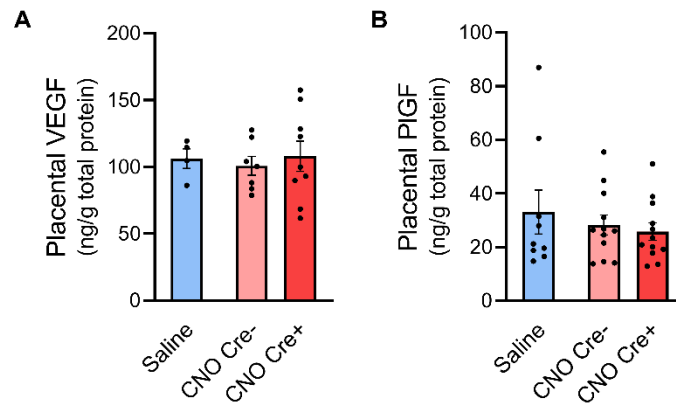


Fig. S9.

Labyrinth-enriched placental expression of angiogenic proteins in *hM3Dq^{F/F}* dam x *Gcm1-Cre^{+/-}* sire pregnancies at GD 14.5.

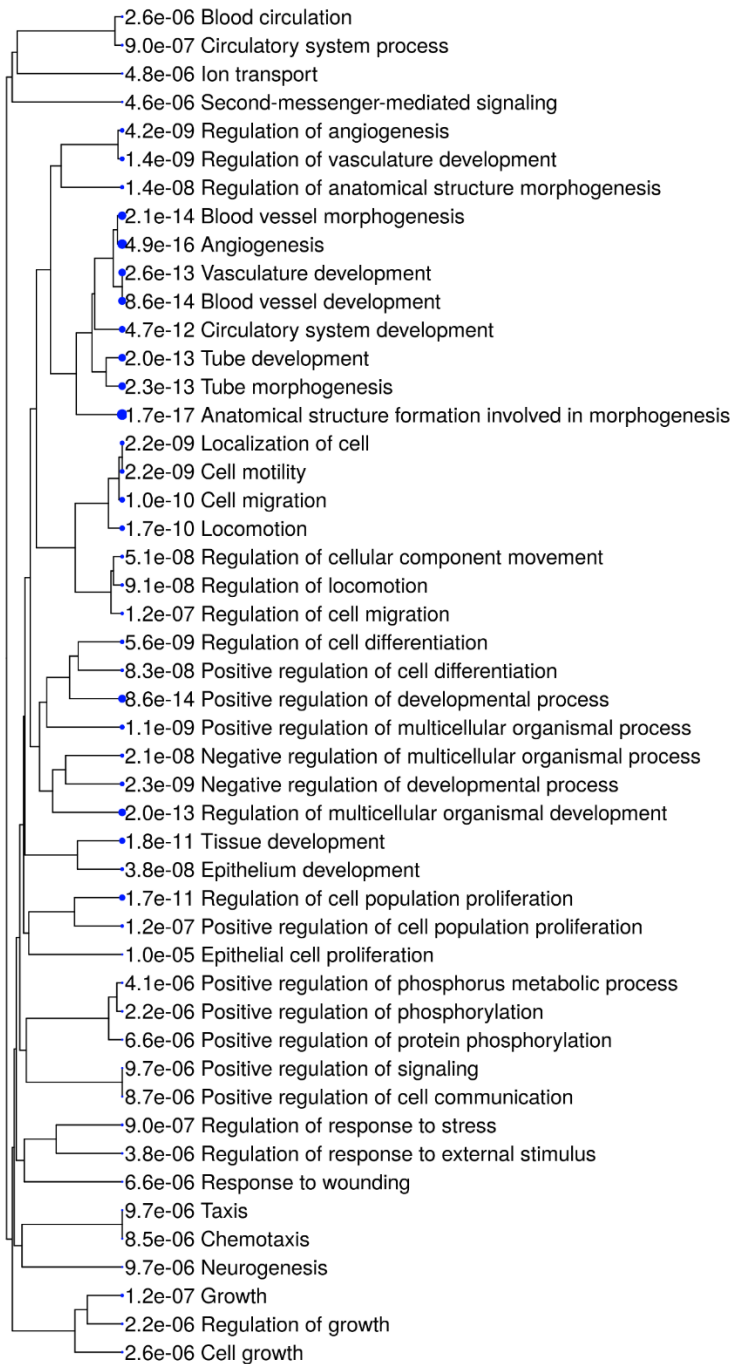


Fig. S10.

Linkage among enriched gene ontology biological processes terms (Shiny GO 0.77) within the differentially expressed gene set of CNO Cre⁺ placentas compared to controls (Saline, CNO Cre⁻) determined by bulk RNA-sequencing sequencing (n=6 per group, hM3Dq^{F/F} dam x *Gcm1*-Cre^{+/-} sire, GD 14.5).

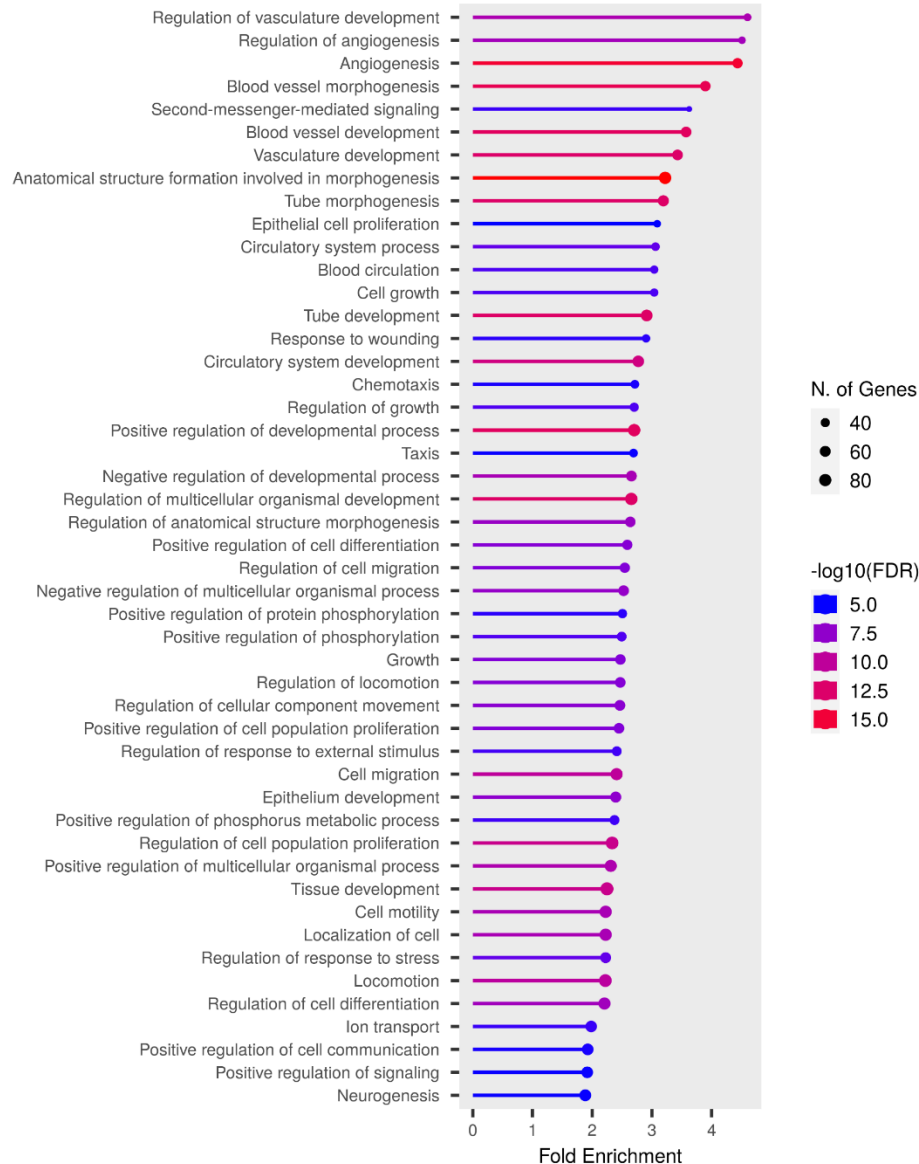


Fig. S11.

Enriched gene ontology biological processes terms (Shiny GO 0.77) within the differentially expressed gene set of CNO Cre⁺ placentas compared to controls (Saline, CNO Cre⁻) determined by bulk RNA-sequencing sequencing (n=6 per group, hM3Dq^{F/F} dam x *Gcm1*-Cre^{+/-} sire, GD 14.5).

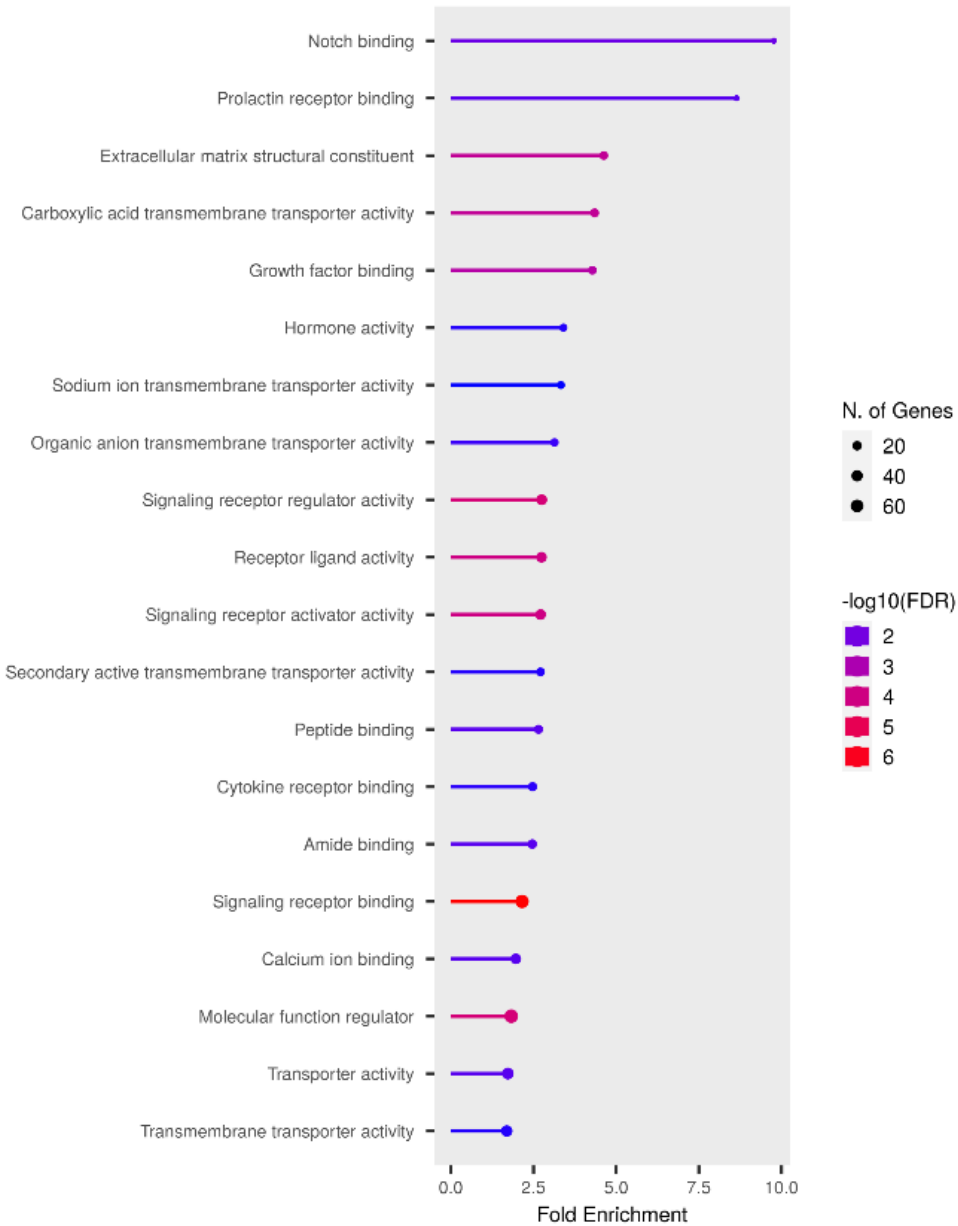


Fig. S12.

Enriched gene ontology molecular function terms (Shiny GO 0.77) within the differentially expressed gene set of CNO Cre⁺ placentas compared to controls (Saline, CNO Cre⁻) determined by bulk RNA-sequencing sequencing (n=6 per group, hM3Dq^{F/F} dam x *Gcm1*-Cre^{+/-} sire, GD 14.5).

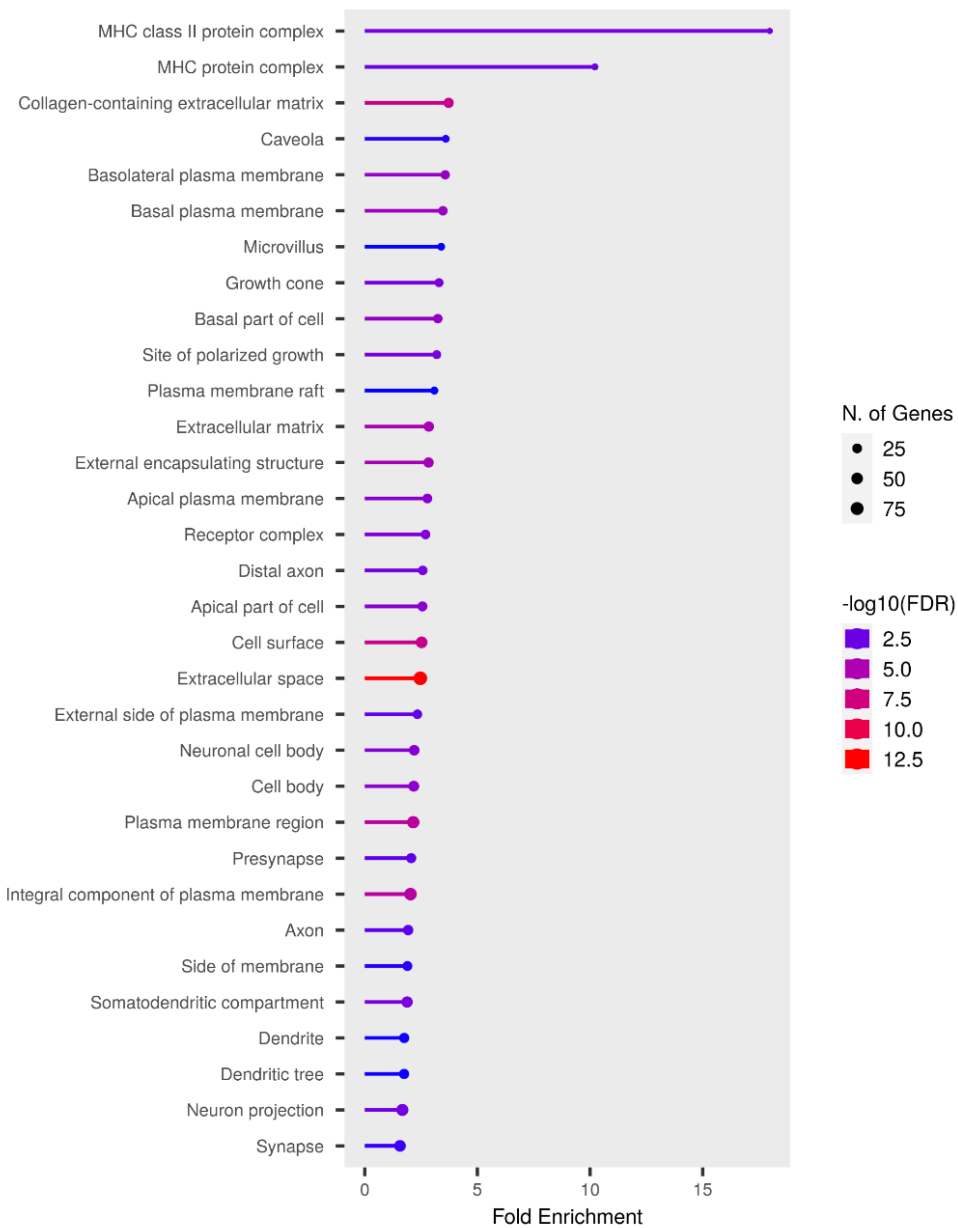


Fig. S13.

Enrichment of various cell compartments (Shiny GO 0.77) within the differentially expressed gene set of CNO Cre⁺ placentas compared to controls (Saline, CNO Cre⁻) determined by bulk RNA-sequencing (n=6 per group, hM3Dq^{F/F} dam x *Gcm1*-Cre^{+/-} sire, GD 14.5).

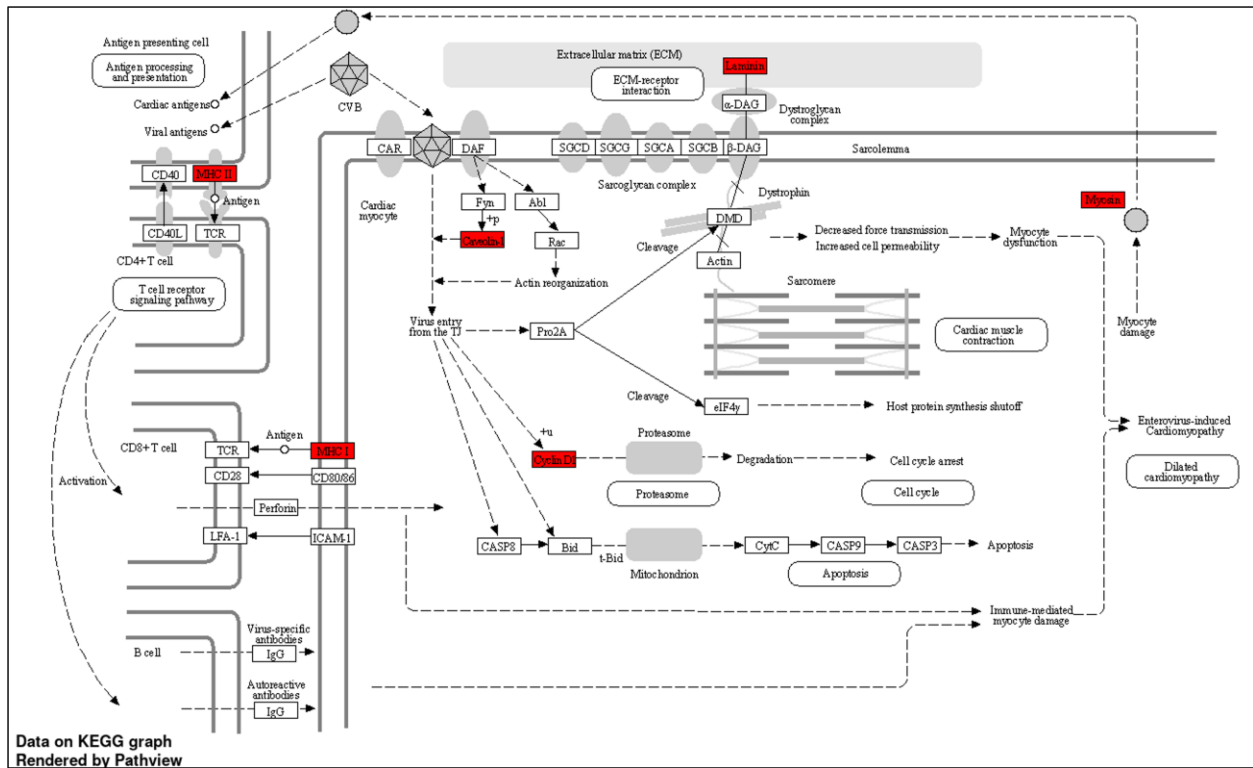


Fig. S14.
KEGG pathway analysis (ShinyGO 0.77) within the differentially expressed gene set in CNO Cre⁺ placenta vs. controls (Saline, CNO Cre⁻) determined by bulk RNA-sequencing (n=6 per group, *hm3Dq*^{F/F} dam x *Gcm1*-Cre^{+/-} sire, GD 14.5). Red indicates enrichment.

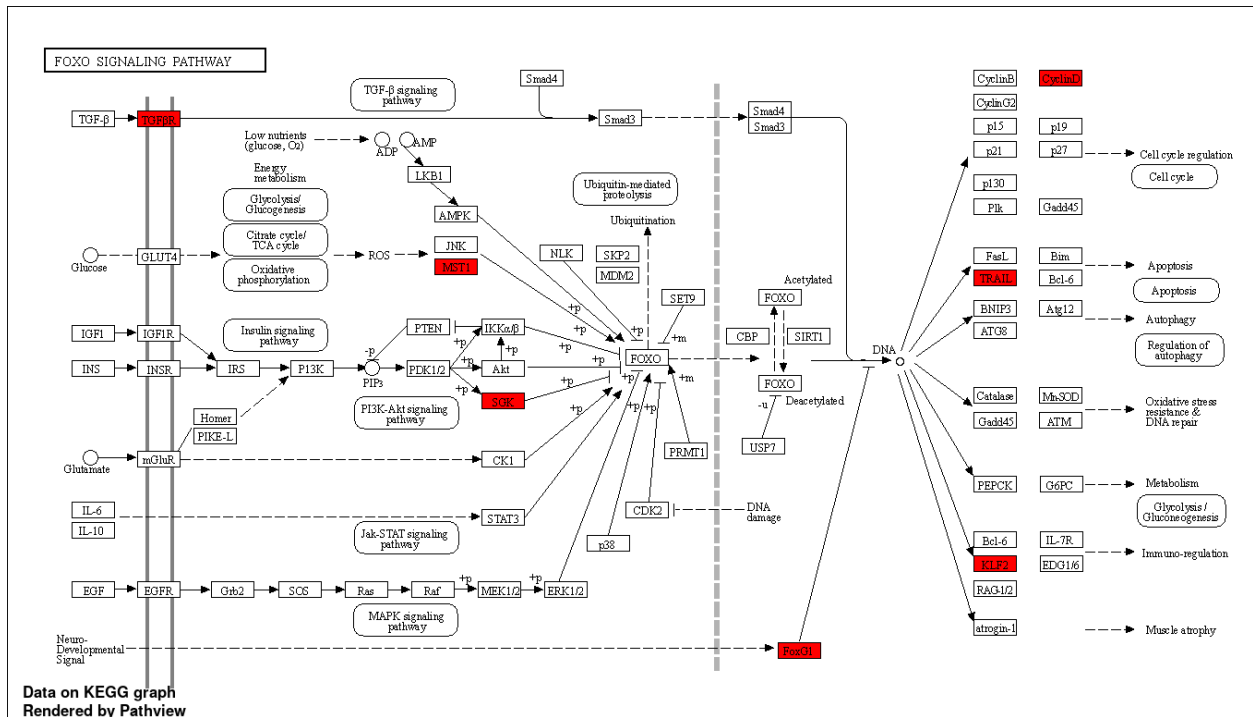


Fig. S15. KEGG pathway analysis for the FOXO signaling pathway (ShinyGO 0.77) within the differentially expressed gene set in CNO Cre⁺ placenta vs. controls (Saline, CNO Cre⁻) determined by bulk RNA-sequencing (n=6 per group, *hM3Dq*^{F/F} dam x *Gcm1*-Cre^{+/-} sire, GD 14.5). Red indicates enrichment.

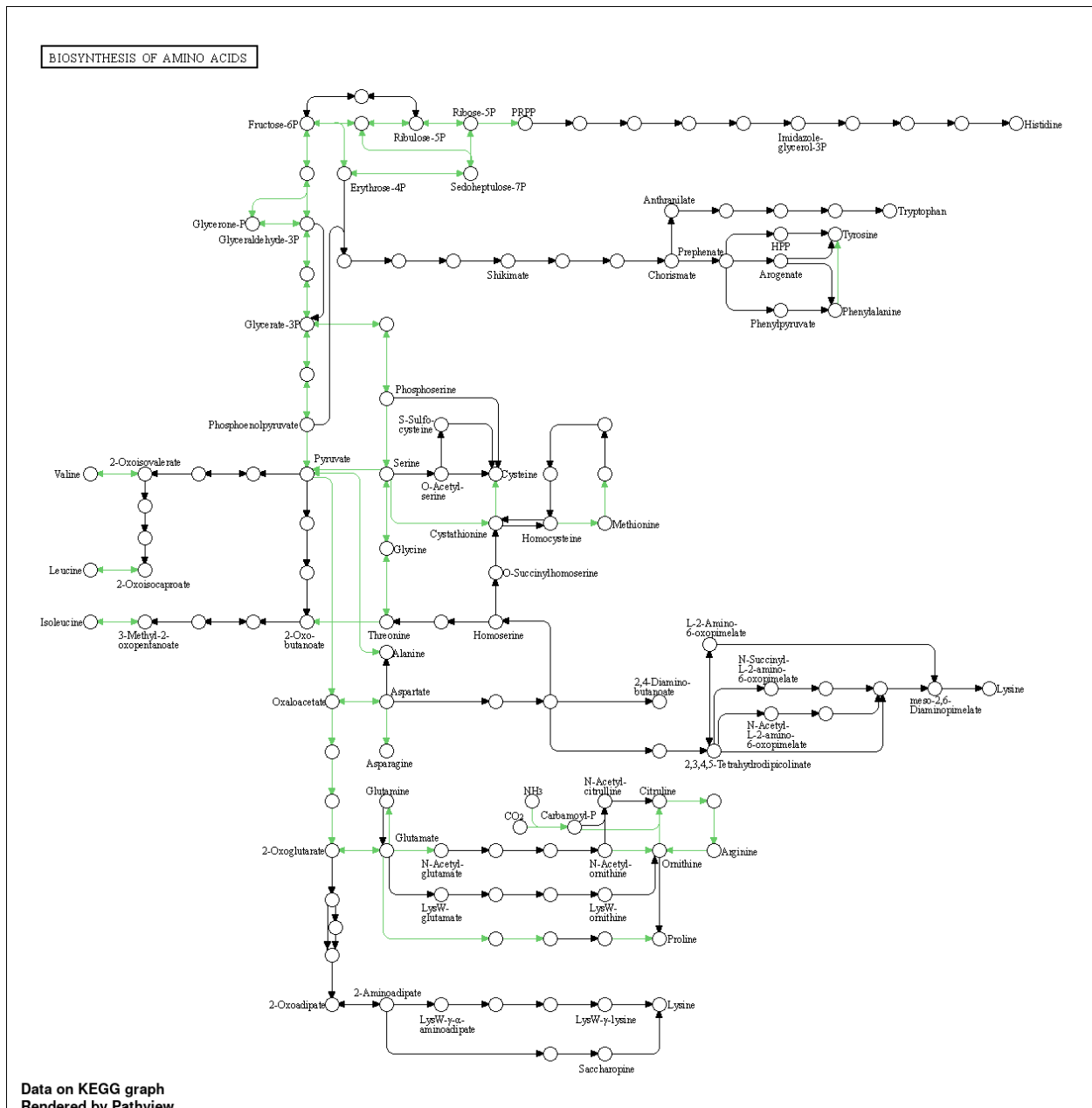
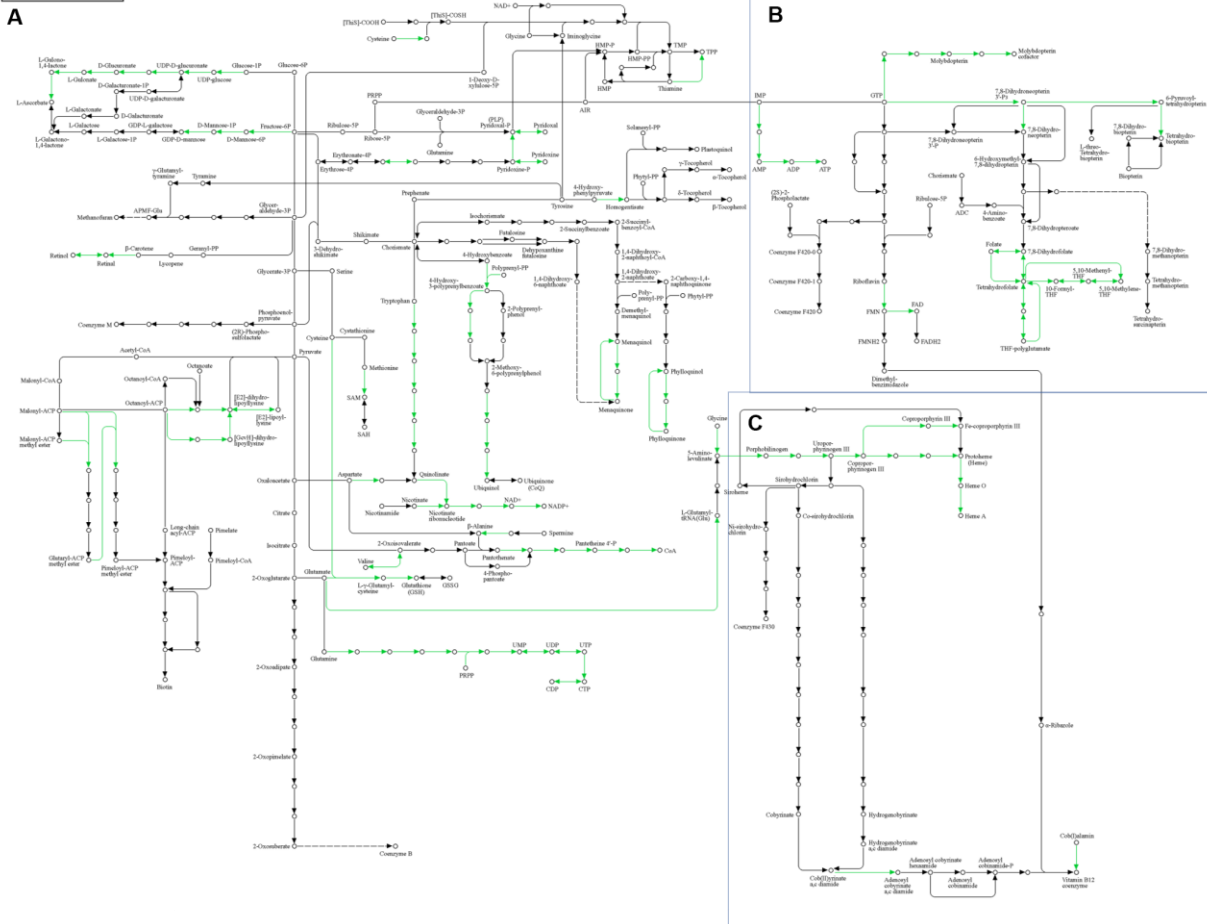


Fig. S16.

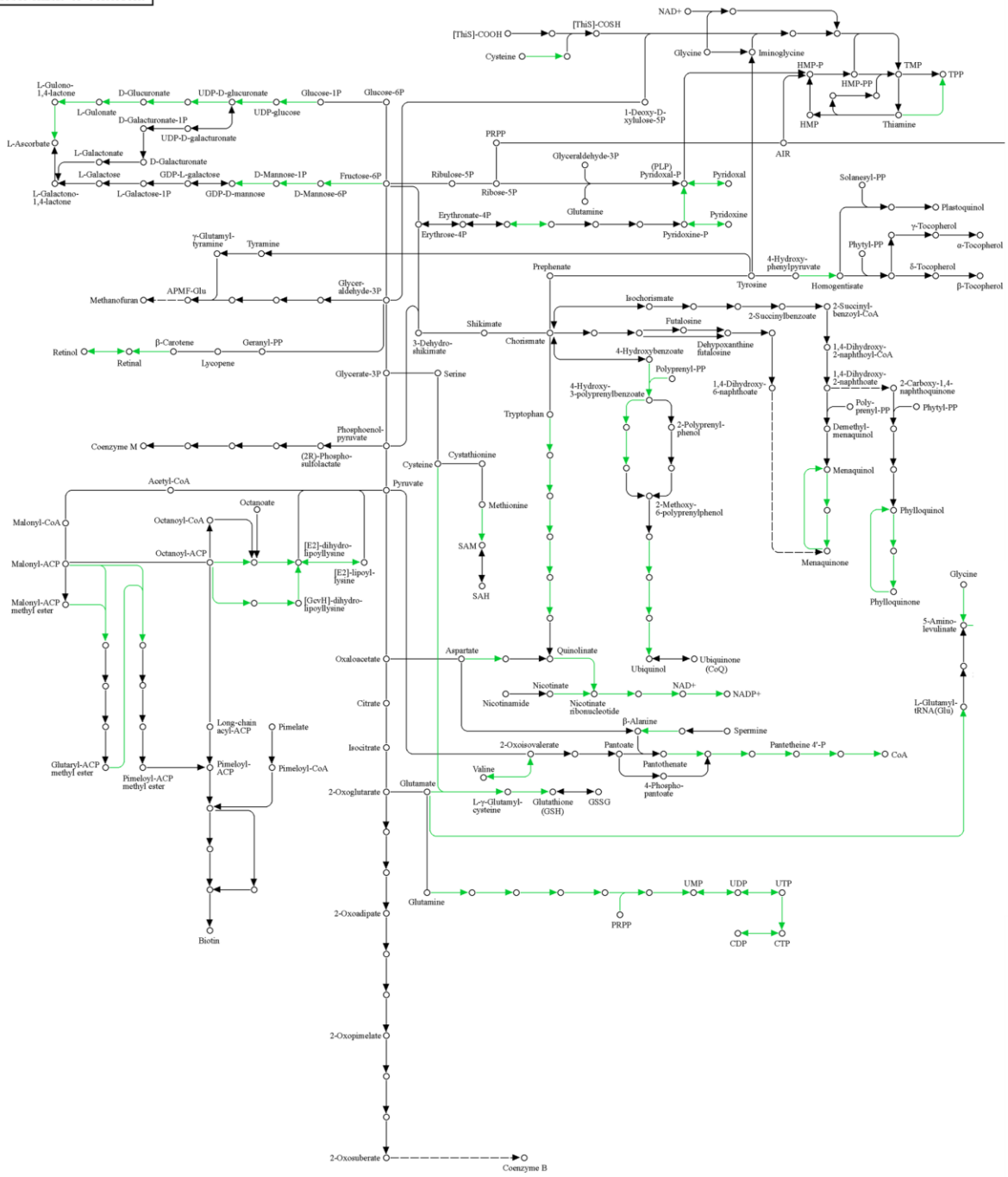
KEGG pathway analysis for biosynthesis of amino acids (ShinyGO 0.77) within the downregulated gene set in CNO Cre⁺ placenta vs. saline determined by bulk RNA-sequencing (n=6 per group, *hM3Dq*^{F/F} dam x *Gcm1*-Cre^{+/-} sire, GD 14.5). Green arrows indicate affected processing.

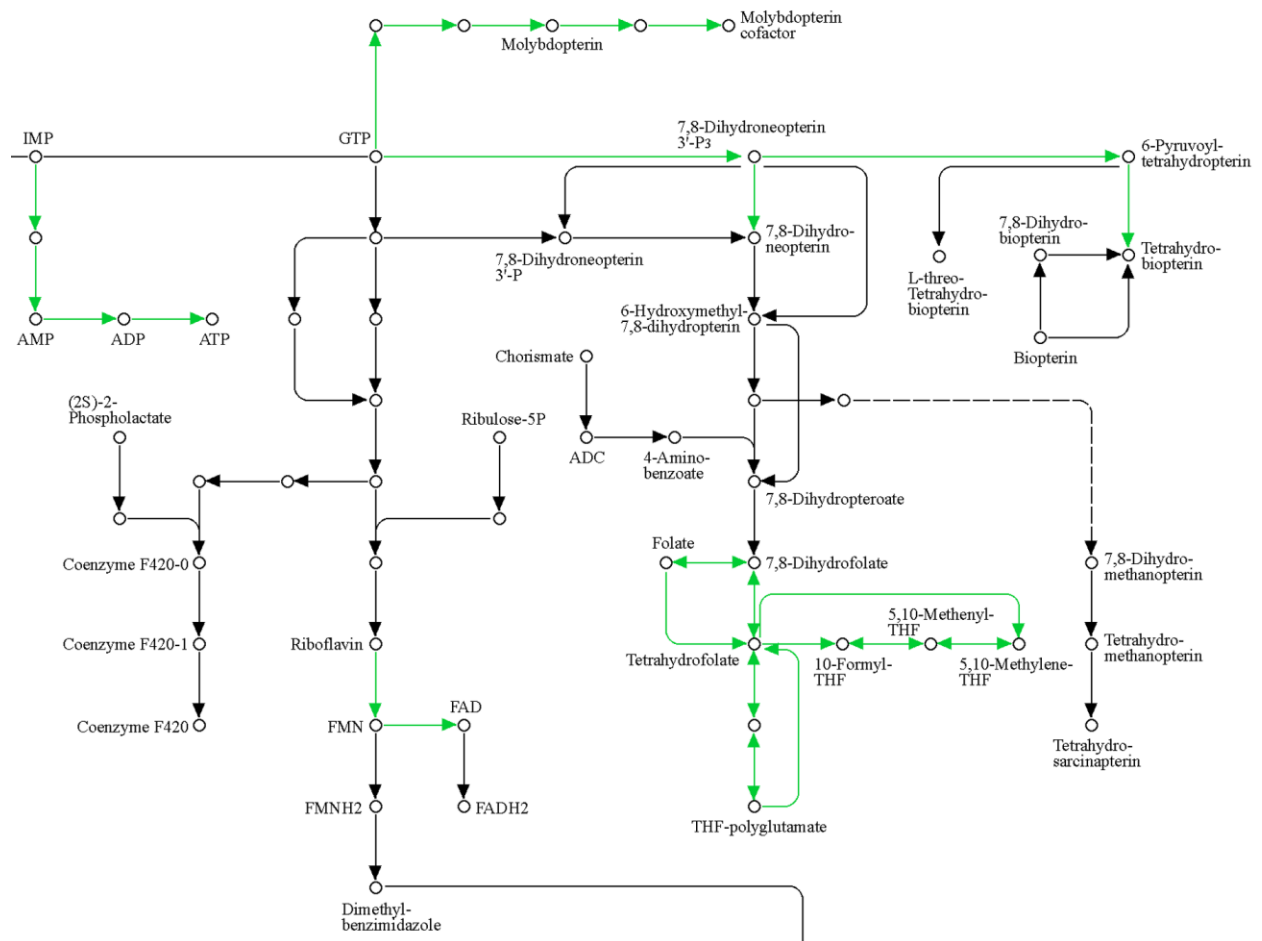
BIOSYNTHESIS OF COFACTORS



BIOSYNTHESIS OF COFACTORS

A



B

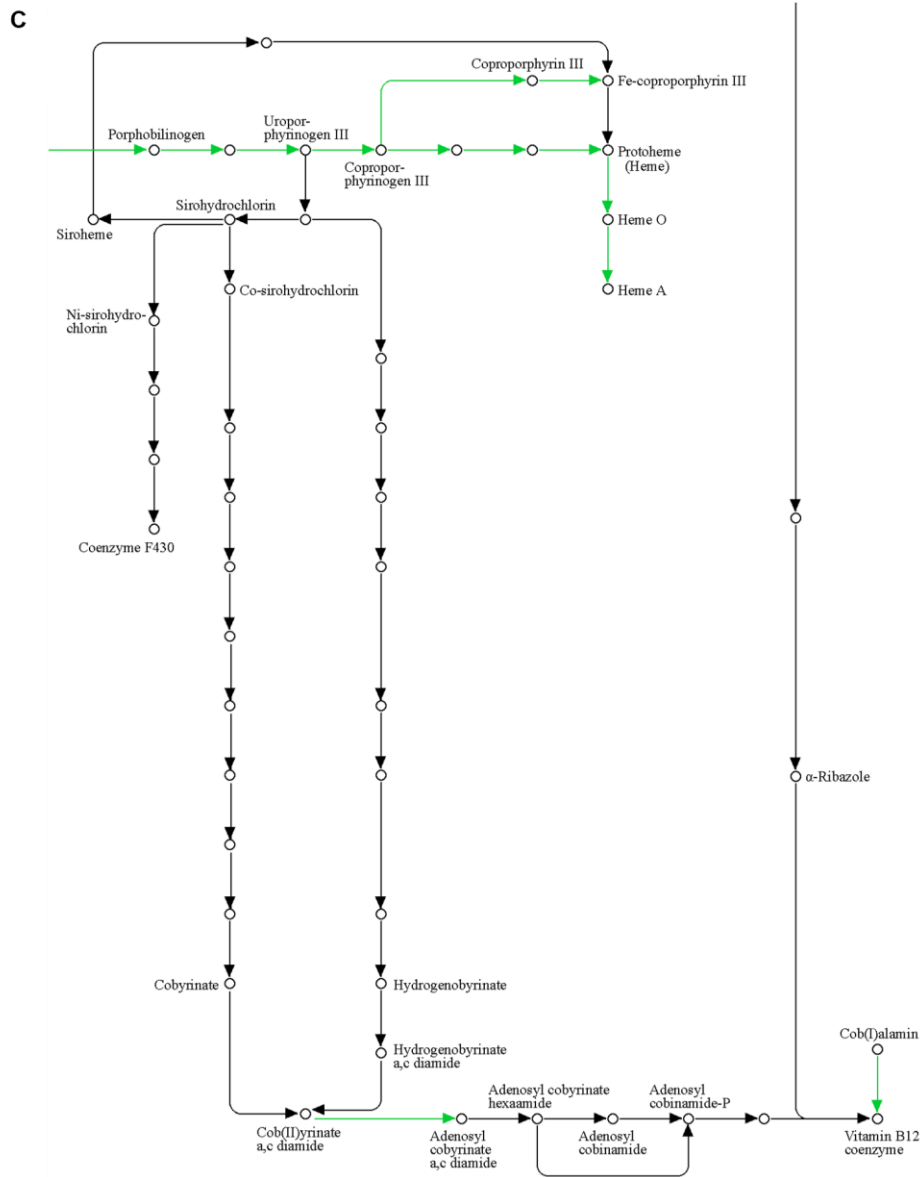


Fig. S17.
KEGG pathway analysis for biosynthesis of cofactors (ShinyGO 0.77) within the downregulated gene set in CNO Cre⁺ placenta vs. saline determined by bulk RNA-sequencing (n=6 per group, *hM3Dq*^{F/F} dam x *Gcm1*-Cre^{+/-} sire, GD 14.5). Green arrows indicate affected processing.

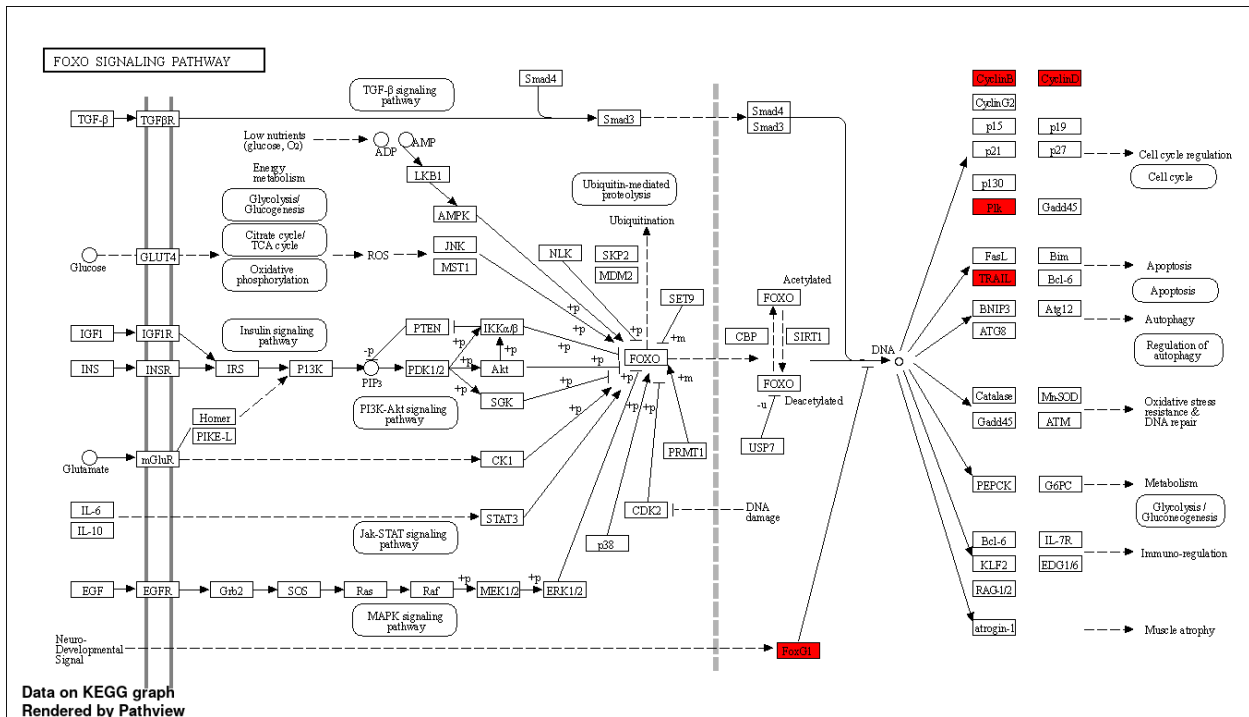


Fig. S18. KEGG pathway analysis for the FOXO signaling pathway (ShinyGO 0.77) within the downregulated gene set in CNO+MitoQ Cre⁺ placenta vs. CNO Cre⁺ determined by bulk RNA-sequencing (n=6 per group, *hM3Dq*^{F/F} dam x *Gcm1*-Cre^{+/-} sire, GD 14.5). Red indicates enrichment.

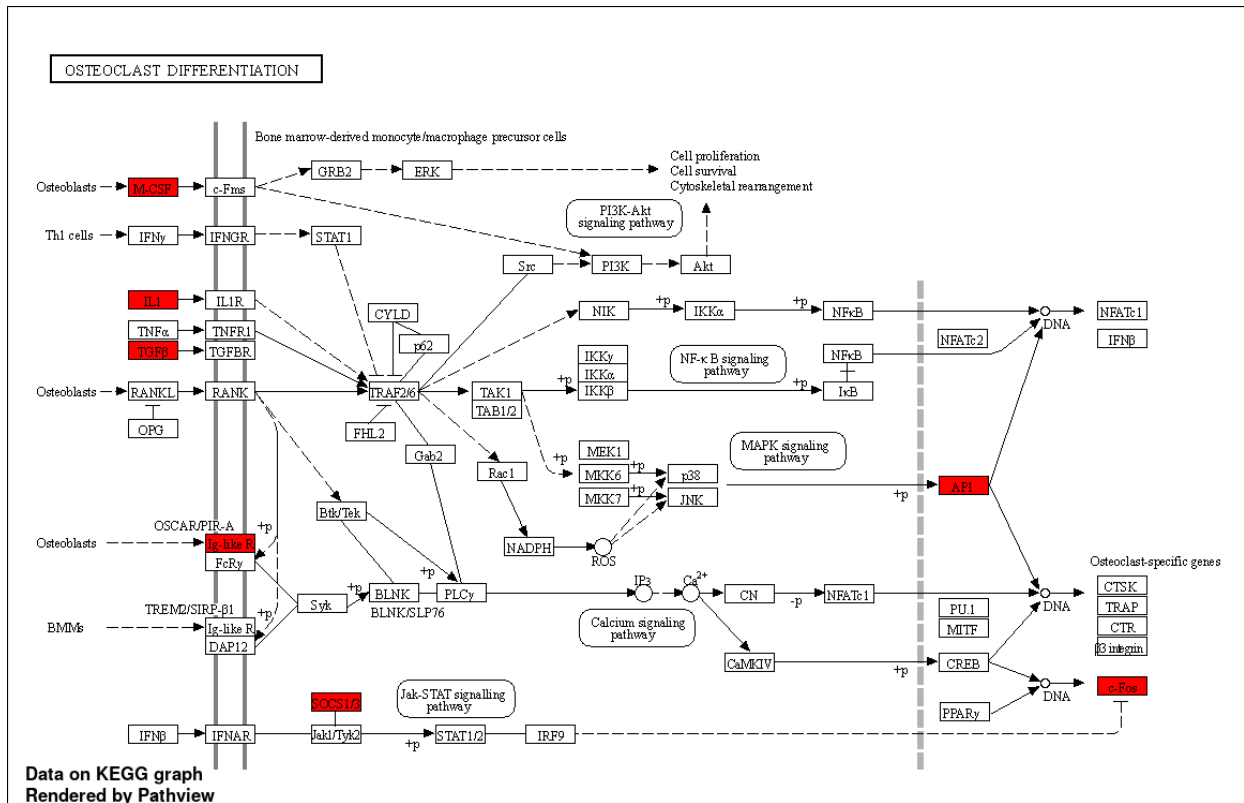


Fig. S19. KEGG pathway analysis for the osteoclast differentiation pathway (ShinyGO 0.77) within the differentially expressed gene set in CNO+MitoQ Cre⁺ placenta vs. CNO Cre⁺ determined by bulk RNA-sequencing (n=6 per group, *hM3Dq*^{F/F} dam x *Gcm1*-Cre^{+/-} sire, GD 14.5). Red indicates enrichment.

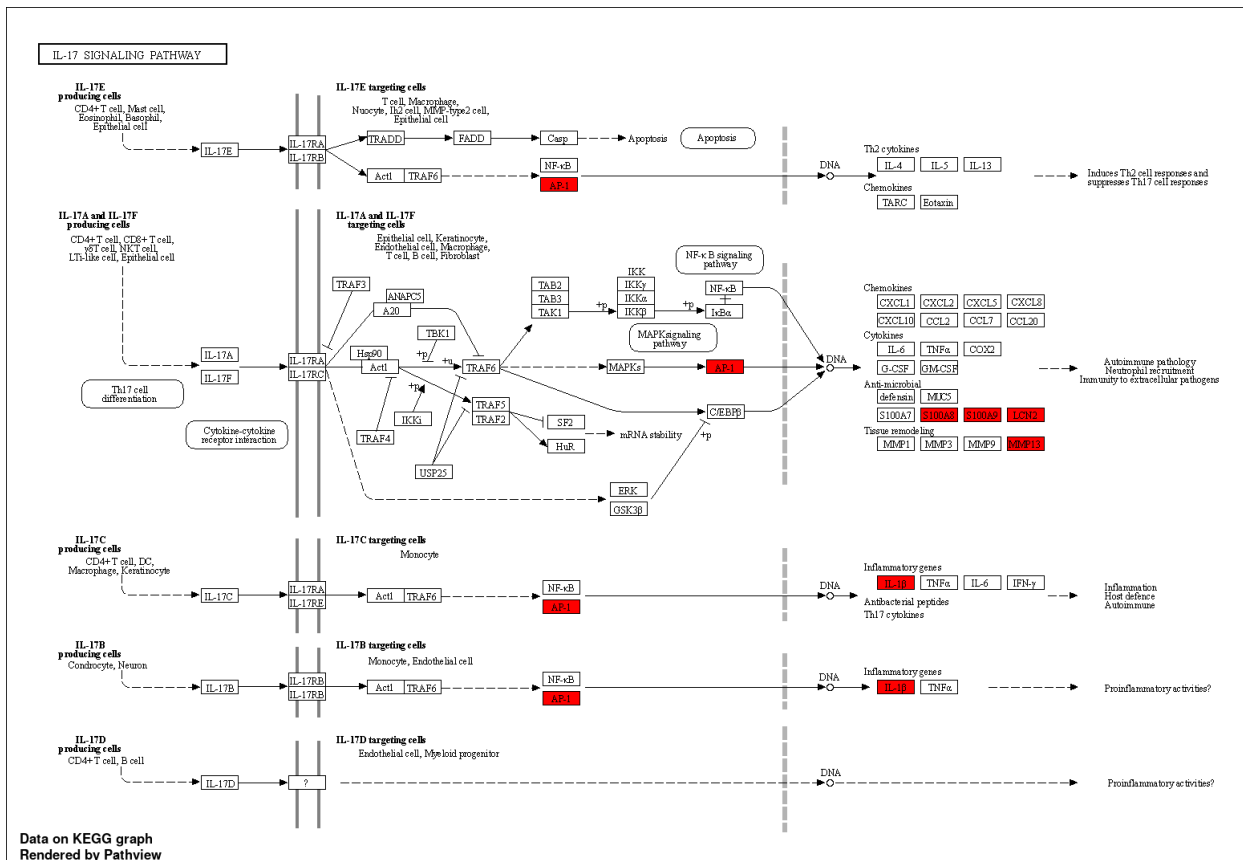


Fig. S20.

KEGG pathway analysis for the IL-17 signaling pathway (ShinyGO 0.77) within the differentially expressed gene set in CNO+MitoQ Cre⁺ placenta vs. CNO Cre⁺ determined by bulk RNA-sequencing (n=6 per group, *hM3Dq*^{F/F} dam x *Gcm1*-Cre^{+/−} sire, GD 14.5). Red indicates enrichment.

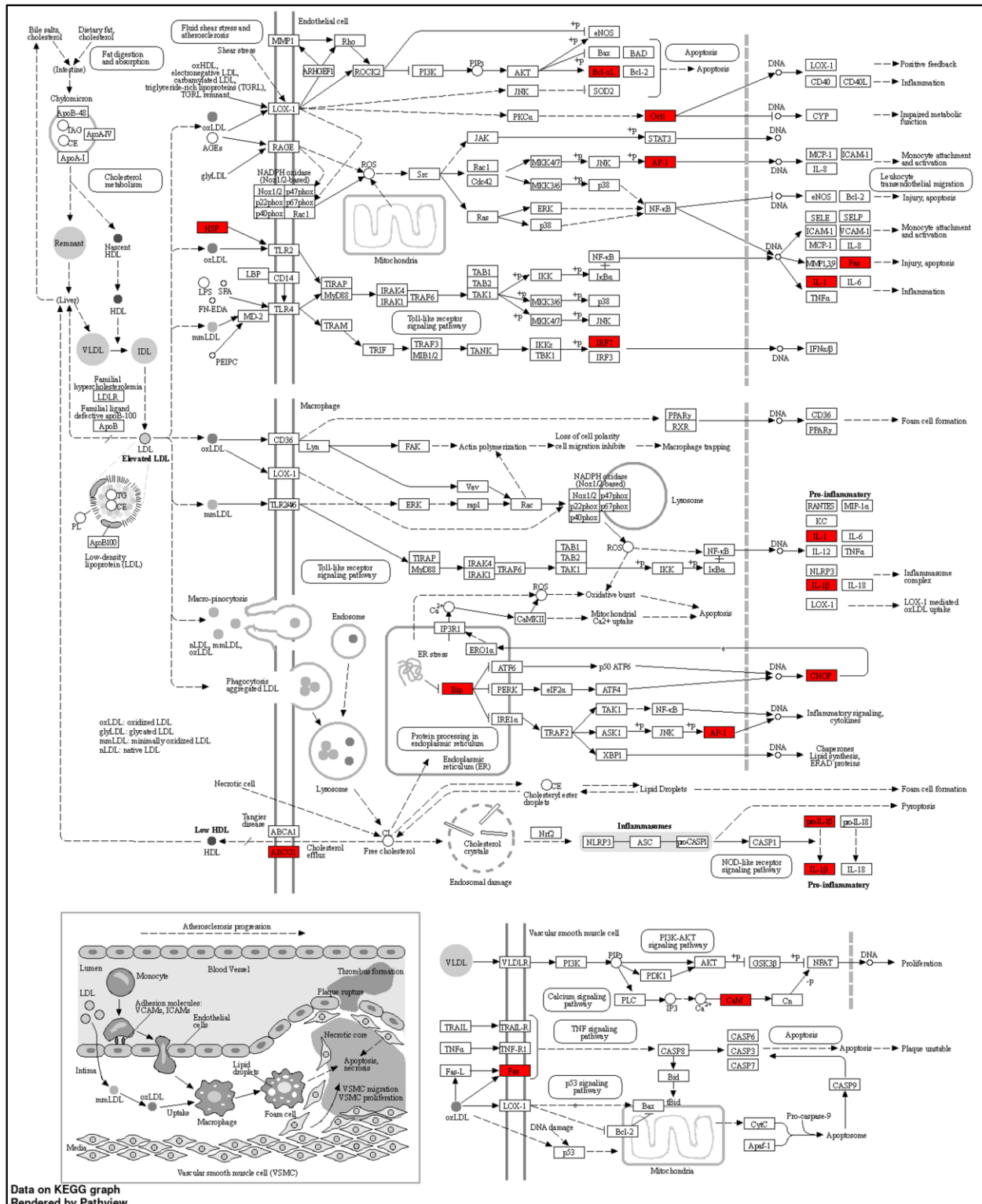


Fig. S21.

KEGG pathway analysis (ShinyGO 0.77) within the differentially expressed gene set in CNO+MitoQ Cre⁺ placenta vs. CNO Cre⁺ determined by bulk RNA-sequencing (n=6 per group, *hm3Dq*^{F/F} dam x *Gcm1*-Cre^{+/-} sire, GD 14.5). Red indicates enrichment.

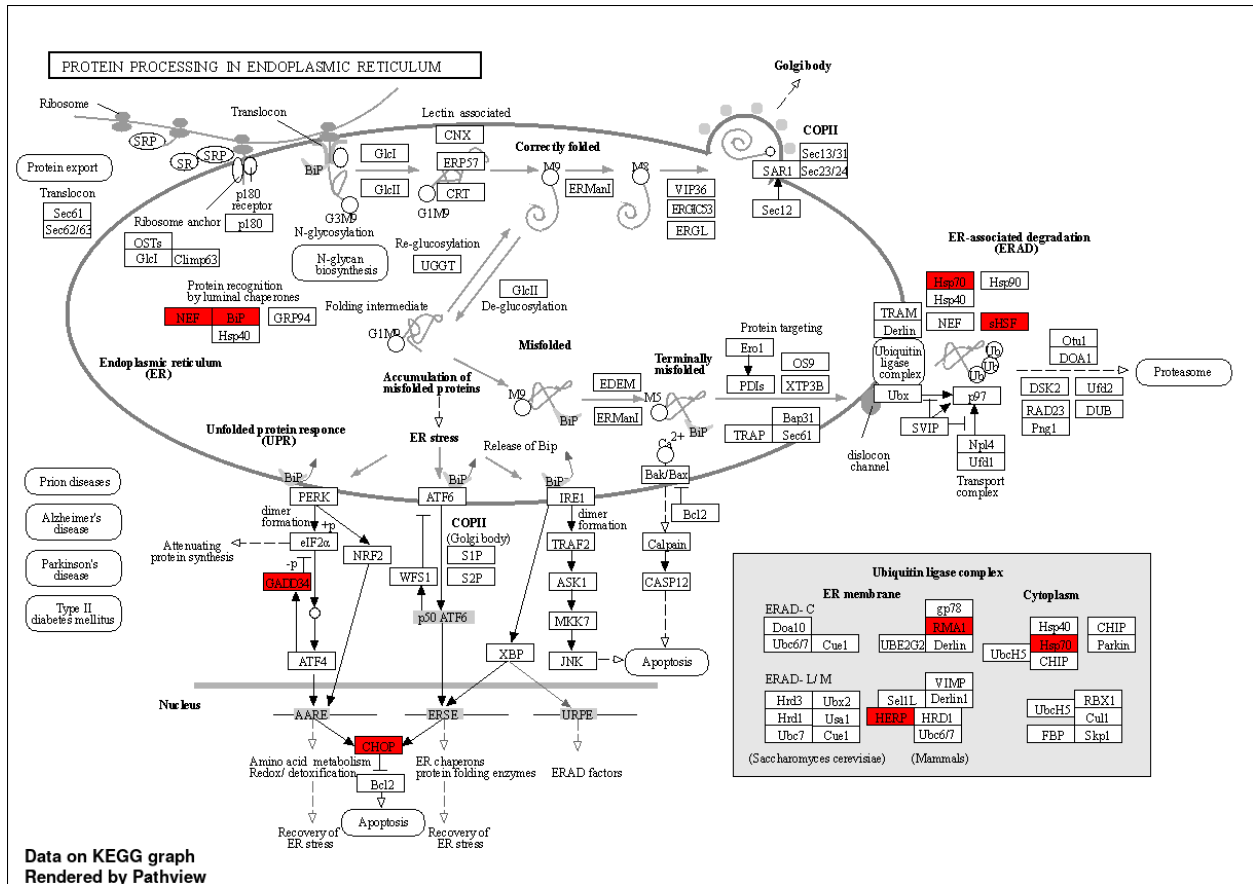


Fig. S22.

KEGG pathway analysis for protein processing in the endoplasmic reticulum (ShinyGO 0.77) within the upregulated gene set in CNO+MitoQ Cre⁺ placenta vs. CNO Cre⁺ determined by bulk RNA-sequencing (n=6 per group, *hM3Dq*^{F/F} dam x *Gcm1*-Cre^{+/-} sire, GD 14.5). Red indicates enrichment.

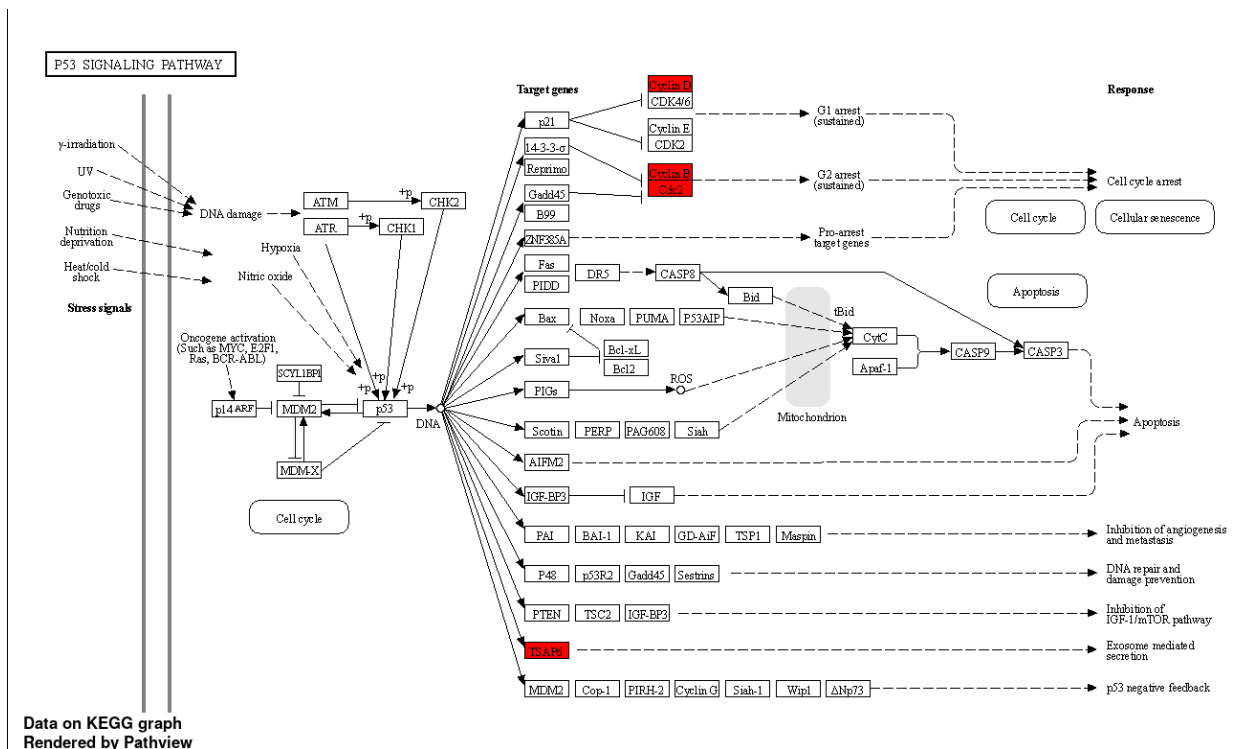


Fig. S23.

KEGG pathway analysis for P53 signaling (ShinyGO 0.77) within the downregulated gene set in CNO+MitoQ Cre⁺ placenta vs. CNO Cre⁺ determined by bulk RNA-sequencing (n=6 per group, *hM3Dq*^{F/F} dam x *Gcm1-Cre*^{+/-} sire, GD 14.5). Red indicates enrichment.

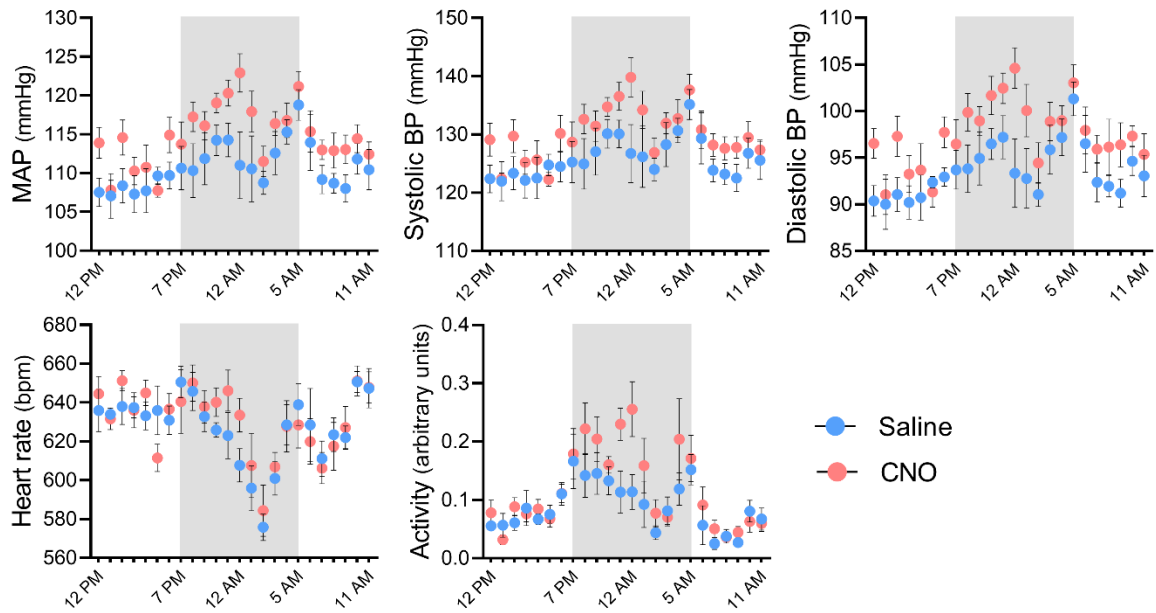


Fig. S24.

Primary maternal hemodynamic parameters in *hM3Dq^{F/F}* dam x *Gcm1-Cre^{+/-}* sire pregnancies. Hourly average from GD 13 to 16.5 (Saline n=6, CNO n=8); MAP, mean arterial pressure. BP, blood pressure.

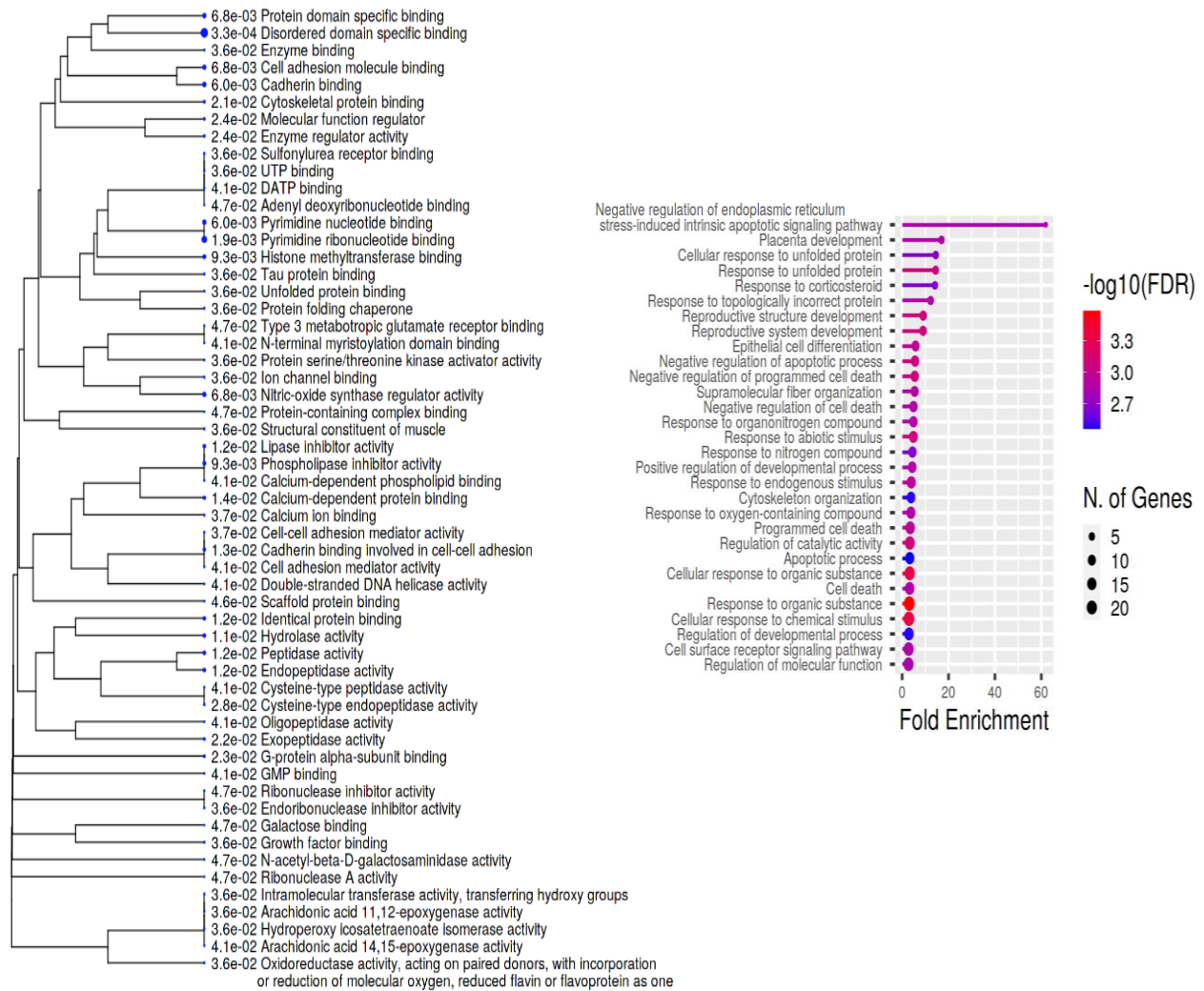
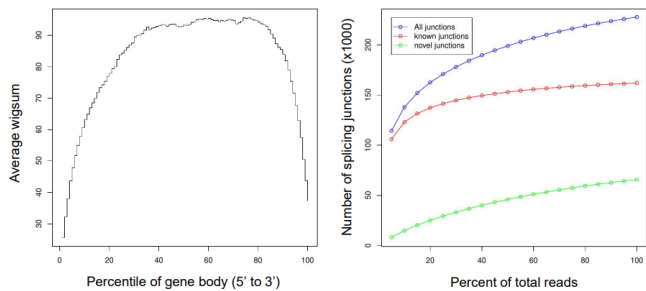
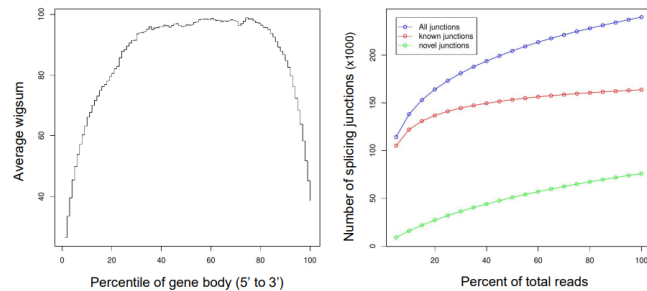


Fig. S25. Upregulated gene ontology molecular function (left) and biological processes terms (right) (ShinyGO 0.74.1) within human preeclamptic syncytiotrophoblasts compared to control syncytiotrophoblasts determined by single-cell RNA sequencing (n=4 per group). Gene set from Zhang et al. (8).

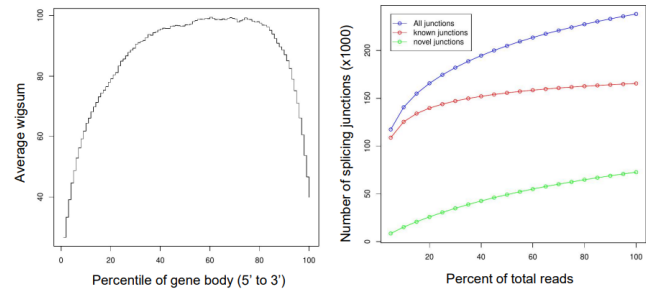
Saline rep1



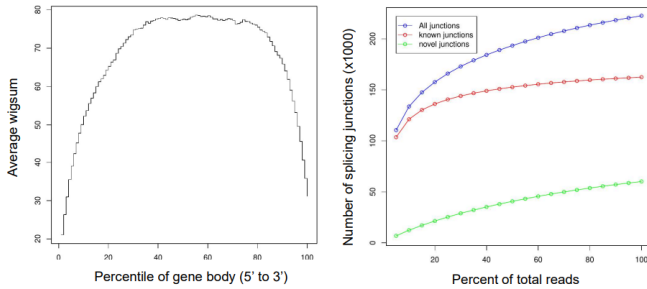
Saline rep2



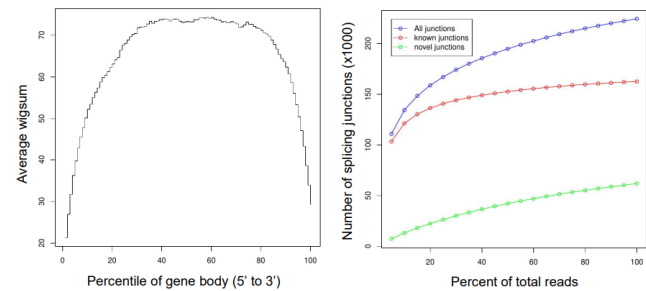
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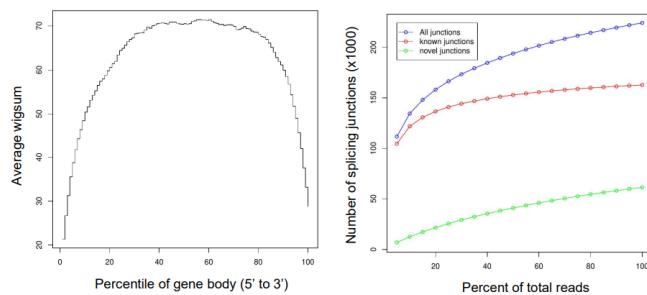
Saline rep4

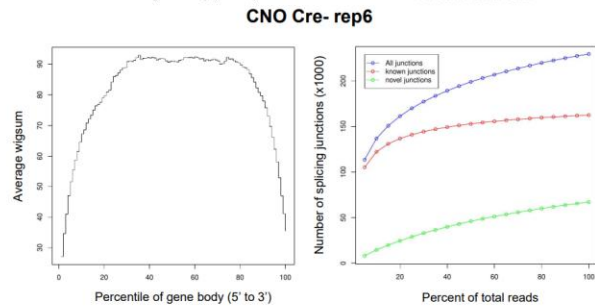
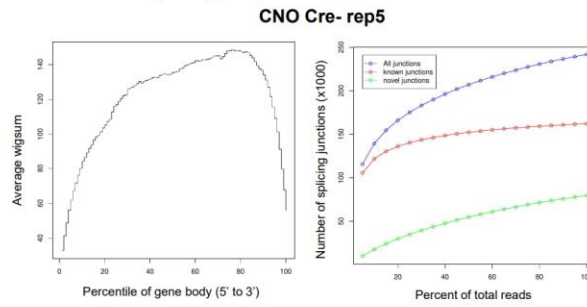
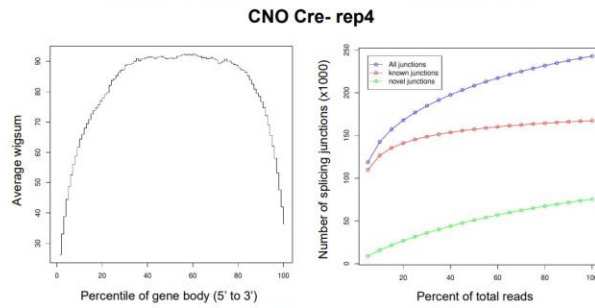
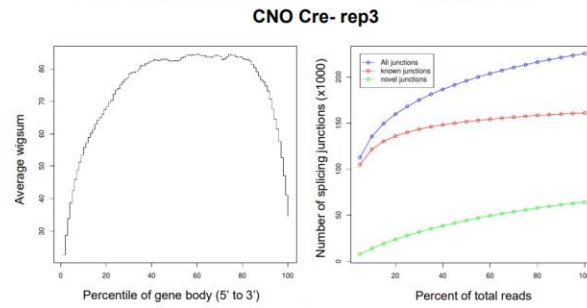
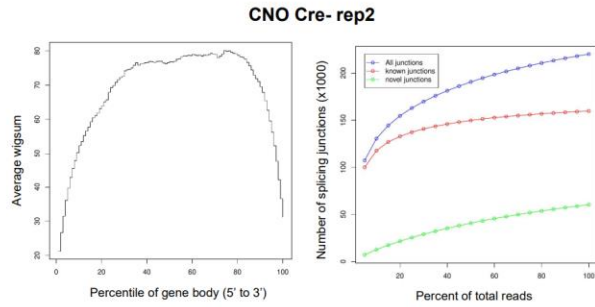
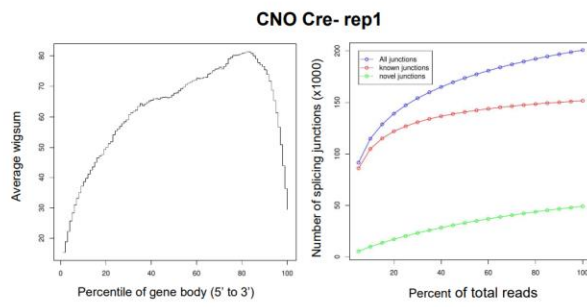


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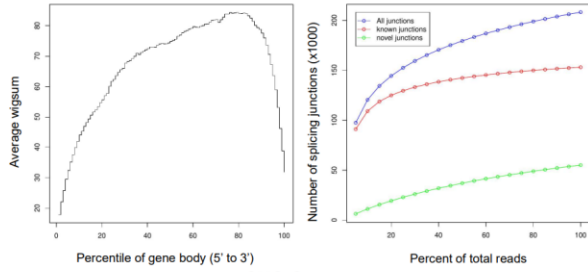


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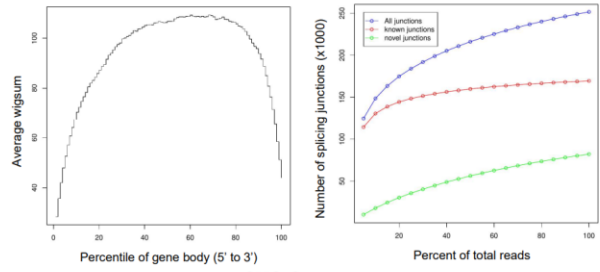




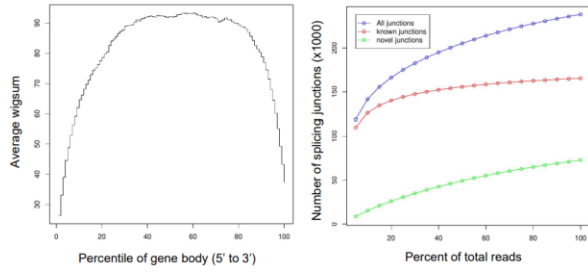
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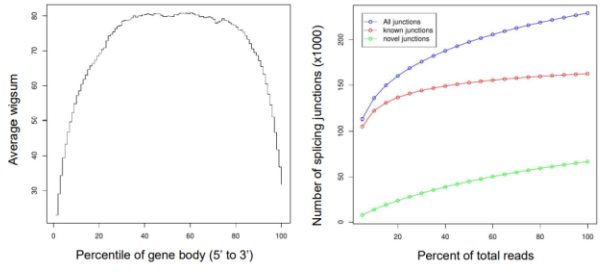
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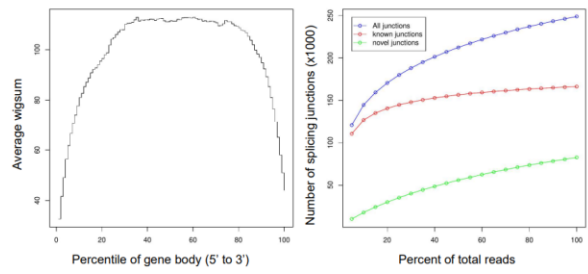
CNO Cre+ rep3



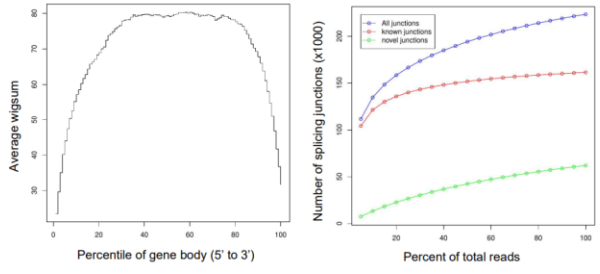
CNO Cre+ rep4



CNO Cre+ rep5



CNO Cre+ rep6



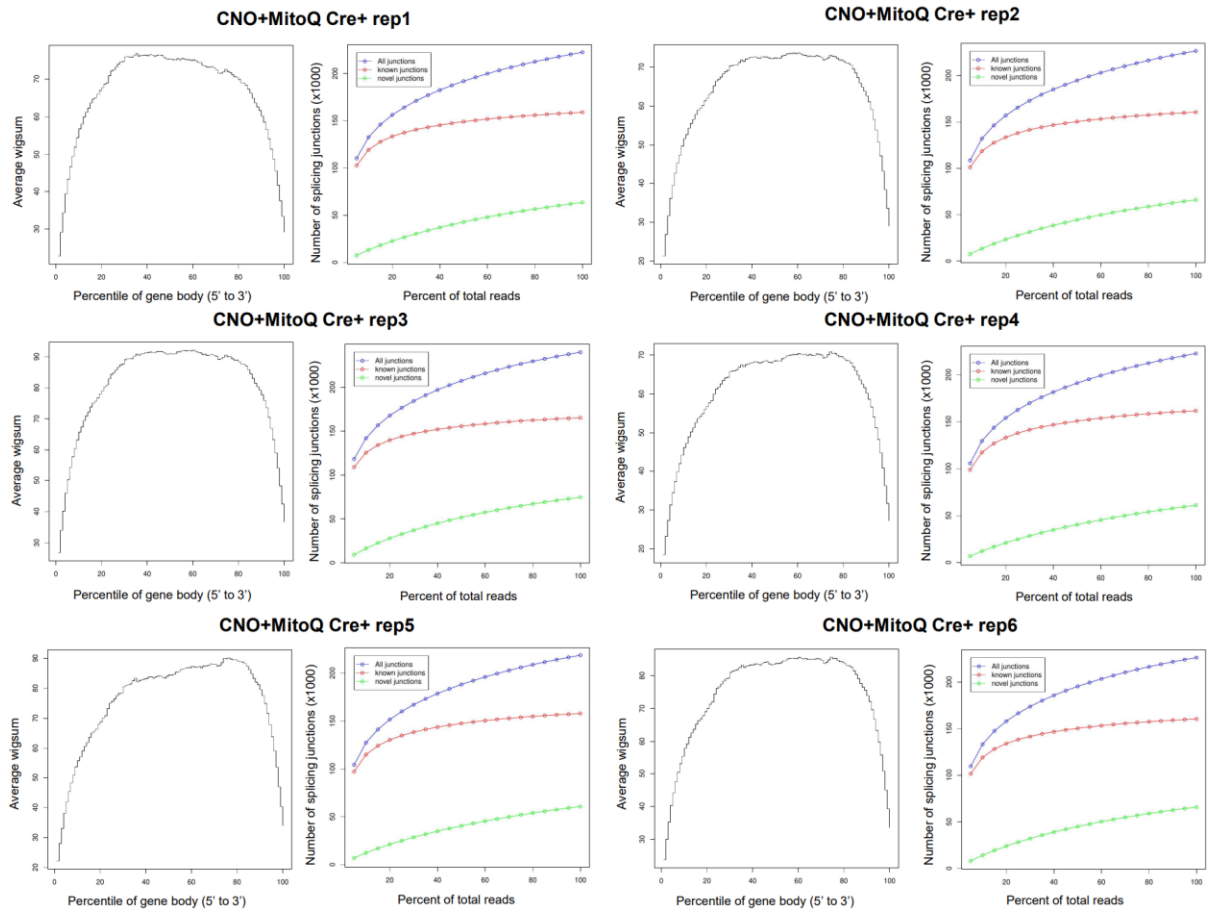


Fig. S26.

RSeQC outputs of aligned bulk RNA-sequencing data from *hM3Dq^{F/F} dam x Gcm1-Cre^{+/-} sire placentas*. Left panels depict gene body coverage and right panels illustrate splice junction saturation plots.

Table S1.

Effect of experimental manipulations on fetoplacental unit numbers and resorptions (Saline n=10, CNO Control n=3, MitoQ Control n=3, CNO n=15, CNO+MitoQ n=8, GD 14.5).

	Saline	CNO Control	MitoQ Control	CNO	CNO + MitoQ
Dam x Sire	<i>hM3Dq</i> ^{F/F} x <i>Gcm1-Cre</i> ^{+/-}	C57BL/6J x <i>Gcm1-Cre</i> ^{+/- or -/-}	C57BL/6J x <i>Gcm1-Cre</i> ^{+/- or -/-}	<i>hM3Dq</i> ^{F/F} x <i>Gcm1-Cre</i> ^{+/-}	<i>hM3Dq</i> ^{F/F} x <i>Gcm1-Cre</i> ^{+/-}
Fetoplacental units per dam	7 (4-9)	8 (5-10)	3 (3-5)	6 (4-8)	6 (4-7)
Resorption count per dam	1 (0-1)	0 (0-1)	0 (0-1)	2 (0-2)	2 (0-2)

Data reported as median (25th-75th percentile)

Table S2.

Differentially expressed HIF1 α target genes within placental RNA-sequencing dataset of *hM3Dq^{F/F}* dam x *Gcm1-Cre^{+/-}* sire pregnancies (n=6 per group, GD 14.5). *Mus Musculus* HIF1 α target genes curated by TFLink (PMID: 36124642). *inferred by curator but not confirmed by chromatin immunoprecipitation assay. **Bold refers to transcripts differentially expressed in both datasets (CNO Cre⁺ vs. Saline and CNO Cre⁺ vs. CNO Cre⁻).**

Differentially Expressed HIF1α Targets (<i>P</i> < 0.05)	
CNO Cre ⁺ vs. Saline	<i>Calcr1, Arl14epl, Pnoc, Arl15, Rgcc, Dcx</i> *, <i>Hsph1, Dmkn, Slc7a6, Abcc1, Psat1, Gm20721, Ets1, Greb1, Foxa1, Sohlh2, Gcat, Fli1, Mthfd1l, Ginn1, Rgs2, Mdk</i> *, <i>Fkbp4, Apold1, Usp2, Klf2, Pigx, Mboat7, Pde4b, Npas2, Mab21l2, Efh2, Mpp2, Dll4</i> *, <i>Triap1, Lap3, Kbtbd6, Gla, Ntml, Ost4, Mfsd5, Rab24, Slc39a13, Larp4, Tasor2, Setd1b, Bdp1, Cbx5, Prr12, Tiam1, Mybl2, Pole, Atad2, Gas2l3, Atad5, Esco2, Zbed6</i>
CNO Cre ⁺ vs. CNO Cre ⁻	<i>Dcx</i> *, <i>Retnla</i> *, <i>Ccnd2, Abcb1b, Rb1, Slc7a6, Mt1, Ets1, Bcl11b, Samd1, Kcnn4, Atf5, Arl15, Tfrc, Bcor1l, Hcfc1r1, Cdk5rap1, Ier3, Mpp7, Plpp5, Ahcy12, Gadd45g, Smim14, Lmna, Ptpn4, Serpine1</i> *, <i>Acsl4</i>

Table S3.

Concentration of immune and cardiovascular factors within maternal plasma in *hM3Dq*^{F/F} dam x *Gcm1-Cre*^{+/-} sire mouse pregnancies (Saline n=5, CNO n=11, CNO+MitoQ n=3, GD 14.5); Data represent mean ± SEM. **P* < 0.05, multiple unpaired *t* tests (2-tailed) of log transformed data.

	Saline	CNO	CNO+MitoQ	<i>P</i> CNO vs. Saline	<i>P</i> CNO+MitoQ vs. CNO
MMP9 (ng/ml)	0.4±0.1	2.2±0.4	3.4±2.2	0.0009*	0.55
LIX (ng/ml)	2±0.3	4.7±0.5	1.1±0.5	0.0002*	0.0003*
IL12p40 (pg/ml)	19±8.3	43±7.9	18±9.5	0.01*	0.03*
MDC (pg/ml)	135±43	288±39	135±22	0.02*	0.049*
IP10 (pg/ml)	116±12	151±7.7	139±19	0.03*	0.51
MCP5 (pg/ml)	178±29	252±19	584±64	0.04*	0.0002*
IL3 (pg/ml)	1.4±0.6	9±4.5	3.4±1.4	0.05	0.73
IL6 (pg/ml)	16±4.2	87±37	352±318	0.07	0.33
PAI1 (ng/ml)	3.6±0.8	5.2±0.5	4.9±1.5	0.07	0.70
TARC (pg/ml)	102±11	159±23	103±16	0.09	0.18
MCSF (pg/ml)	24±4.2	37±5.2	28±4.7	0.11	0.42
Eotaxin (pg/ml)	562±69	700±51	517±59	0.14	0.10
TNFα (pg/ml)	12±3.2	79±61	11±2.9	0.15	0.34
IFNγ (pg/ml)	8.8±5.9	9.6±2.4	6.5±1.3	0.15	0.63
MIG (pg/ml)	544±55	755±60	590±119	0.16	0.39
IL13 (pg/ml)	70±19	100±19	101±8.2	0.19	0.68
IL1β (pg/ml)	5.2±1.6	979±963	6.6±1.2	0.20	0.47
EPO (pg/ml)	843±500	366±38	453±77	0.26	0.29
GMCSF (pg/ml)	16±3.8	20±2.6	23±1.5	0.27	0.43
IL17 (pg/ml)	12±7.1	34±21	9.9±3.1	0.27	0.61
RANTES (pg/ml)	25±6.1	207±164	24±5.5	0.27	0.53
TIMP1 (ng/ml)	6.8±1.8	4.8±0.7	26±13	0.28	0.00
IL10 (pg/ml)	8.5±0.6	315±294	9.8±4.9	0.29	0.32
IL1α (pg/ml)	186±31	357±77	218±88	0.29	0.41
MIP1β (pg/ml)	123±26	137±8.7	132±19	0.29	0.78
IL4 (pg/ml)	0.8±0.2	76±73	0.5±0.08	0.30	0.31
MIP3α (pg/ml)	107±10	182±53	284±183	0.30	0.59
IFNβ1 (pg/ml)	132±25	196±45	148±22	0.32	0.74
MCP1 (pg/ml)	76±18	299±195	87±30	0.35	0.46
MIP3β (pg/ml)	220±18	238±11	366±78	0.36	0.01*
IL12p70 (ng/ml)	0.04±0.01	1.7±1.6	0.04±0.02	0.38	0.38
Thrombomodulin (ng/ml)	18±4.7	22±2.7	11±7.2	0.38	0.06

KC (pg/ml)	115±29.3	129±21	335±218	0.48	0.20
LIF (pg/ml)	3±2.4	0.9±0.4	0.6±0.5	0.50	0.82
Pecam1 (ng/ml)	1.8±1.1	2±0.4	2±0.4	0.50	0.72
MIP2 (pg/ml)	265±35	324±39	236±49	0.57	0.36
sICAM (ng/ml)	3.5±0.5	3.9±0.3	3.9±0.6	0.58	0.91
sPSelectin (ng/ml)	68±8.7	77±10	75±14	0.63	0.97
IL5 (pg/ml)	30±15	55±43	6.4±0.7	0.69	0.28
MIP1 α (pg/ml)	97±30	99±14	104±14	0.71	0.66
IL16 (ng/ml)	29±14	23±6.8	50±28	0.72	0.19
VEGF (pg/ml)	1.7±1	1.3±0.2	0.9±0.06	0.73	0.41
Fractalkine (pg/ml)	345±65	372±57	263±55	0.77	0.26
sESelectin (ng/ml)	24±6	25±3.2	27±6.3	0.84	0.76
IL9 (pg/ml)	71±17	69±6.5	67±6.2	0.84	0.98
IL15 (pg/ml)	70±30	130±55	42±17	0.84	0.57
IL20 (pg/ml)	104±18	107±22	114±28	0.87	0.67
IL11 (pg/ml)	47±13	51±15	28±8.1	0.93	0.52
IL7 (pg/ml)	10±4.6	15±6.8	3.3±3.3	0.96	0.08
GCSF (ng/ml)	1±0.2	1.1±0.2	2.9±0.5	0.97	0.01*
IL2 (pg/ml)	15±8.5	13±3	6±2.7	0.97	0.15

Table S4.

Concentration of immune and cardiovascular factors within maternal plasma during human preeclampsia (Control n=10, All PreE n=10, “Non-Severe” PreE n=4, Severe PreE=6); Data represent mean \pm SEM. * $P < 0.05$, multiple unpaired t tests (2-tailed) of log transformed data. PreE, preeclampsia.

	Control	All PreE	“Non-Severe” PreE	Severe PreE	P All PreE vs. Control	P Severe PreE vs. “Non-Severe” PreE
MIP1 β (pg/ml)	21 \pm 2	35 \pm 4.3	26 \pm 3.8	40 \pm 5.9	0.01*	0.16
IL6 (pg/ml)	4.2 \pm 0.2	3.4 \pm 0.9	4.9 \pm 1.4	2.4 \pm 1	0.02*	0.14
MMP7 (pg/ml)	234 \pm 37	365 \pm 47	345 \pm 40	374 \pm 67	0.03*	0.95
IL12p40 (pg/ml)	62 \pm 3.2	115 \pm 27	165 \pm 59	81 \pm 16	0.048*	0.17
TIMP2 (ng/ml)	96 \pm 4.1	112 \pm 6.3	100 \pm 9.3	117 \pm 7.5	0.05	0.20
I309 (pg/ml)	0.8 \pm 0.1	1.5 \pm 0.4	1.6 \pm 0.9	1.5 \pm 0.3	0.06	0.58
MMP2 (ng/ml)	82 \pm 5.5	134 \pm 33	83 \pm 11	156 \pm 46	0.07	0.21
TIMP1 (ng/ml)	56 \pm 3.2	70 \pm 6.9	77 \pm 21	66 \pm 5.7	0.07	0.60
Eotaxin (pg/ml)	16 \pm 1.2	19 \pm 0.8	18 \pm 1	19 \pm 1.1	0.10	0.39
TARC (pg/ml)	4.7 \pm 1.1	8.5 \pm 1.9	7.9 \pm 2.9	8.9 \pm 2.7	0.11	0.85
IP10 (pg/ml)	110 \pm 22	245 \pm 99	96 \pm 15	344 \pm 157	0.12	0.08
CTACK (pg/ml)	372 \pm 53	505 \pm 69	442 \pm 110	546 \pm 93	0.15	0.40
MCP4 (pg/ml)	12 \pm 3.7	18 \pm 4.8	11 \pm 4.5	23 \pm 7	0.18	0.14
Eotaxin2 (pg/ml)	133 \pm 36.3	246 \pm 70	193 \pm 46	282 \pm 114	0.19	0.95
TNF β (pg/ml)	7 \pm 5.1	12 \pm 5	13 \pm 0.4	12 \pm 9.1	0.20	0.54
MMP10 (ng/ml)	1.5 \pm 0.2	2.3 \pm 0.5	2.2 \pm 0.9	2.4 \pm 0.6	0.25	0.99
IL21 (pg/ml)	7.5 \pm 2.6	4.5 \pm 1.2	4.4 \pm 1.9	4.6 \pm 1.7	0.27	0.80
MCP1 (pg/ml)	161 \pm 17	225 \pm 35	236 \pm 54	218 \pm 51	0.27	0.66
MIP1 δ (ng/ml)	1.9 \pm 0.2	2.5 \pm 0.4	2.4 \pm 0.9	2.5 \pm 0.4	0.29	0.79
MMP3 (ng/ml)	7.3 \pm 1	11.7 \pm 2.5	10.1 \pm 4.2	12.4 \pm 3.3	0.31	0.85
IFN γ (pg/ml)	6.7 \pm 5.3	11 \pm 4.6	13 \pm 6	8.9 \pm 7.3	0.31	0.37
IL27 (ng/ml)	57 \pm 11	398 \pm 135	740 \pm 114	193 \pm 138	0.31	0.048*
IL8 (pg/ml)	1 \pm 0.2	2.8 \pm 1.4	4.6 \pm 3.5	1.6 \pm 0.5	0.33	0.41
GMCSF (pg/ml)	44 \pm 5.3	74 \pm 25	68 \pm 16	77 \pm 41	0.34	0.63
IL15 (pg/ml)	19 \pm 16	13 \pm 6.9	20 \pm 16	7.8 \pm 1.4	0.38	0.90
IL1 β (pg/ml)	162 \pm 88	82 \pm 29	136 \pm 67	47 \pm 11	0.38	0.10
Fractalkine (pg/ml)	161 \pm 17	192 \pm 27	233 \pm 52	165 \pm 28	0.39	0.23
LIF (pg/ml)	6 \pm 1.6	6.8 \pm 1.6	5.8 \pm 1.7	7.5 \pm 2.6	0.40	0.63
TGF α (pg/ml)	36 \pm 29	105 \pm 94	245 \pm 237	13 \pm 2.7	0.42	0.50
IL5 (pg/ml)	4.3 \pm 1	6.9 \pm 2.1	10 \pm 5	5.2 \pm 0.4	0.44	0.57
IL1RA (pg/ml)	23 \pm 8.6	23 \pm 5.9	32 \pm 14	17 \pm 3.4	0.45	0.30
TNF α (pg/ml)	41 \pm 4.8	62 \pm 17	59 \pm 19	64 \pm 27	0.46	0.75

SDF1 α + β (ng/ml)	1.8 \pm 0.2	1.5 \pm 0.3	1.5 \pm 0.4	1.6 \pm 0.4	0.48	0.87
GRO α (pg/ml)	16 \pm 5.9	10 \pm 3.5	15 \pm 7.6	6.8 \pm 1.6	0.48	0.26
sCD40L (pg/ml)	643 \pm 229	735 \pm 152	762 \pm 314	717 \pm 172	0.49	0.75
IL1 α (pg/ml)	273 \pm 170	168 \pm 91	279 \pm 226	94 \pm 42	0.50	0.48
IL17A (pg/ml)	36 \pm 24	21 \pm 12	37 \pm 29	9.6 \pm 1.6	0.52	0.44
FLT3L (pg/ml)	7.5 \pm 1.3	10 \pm 2.2	12 \pm 4.8	9 \pm 2.2	0.52	0.67
IL16 (pg/ml)	359 \pm 163	383 \pm 142	416 \pm 364	366 \pm 147	0.54	0.47
TSLP (pg/ml)	73 \pm 70	28 \pm 16	39 \pm 35	21 \pm 14	0.54	0.98
IL18 (pg/ml)	377 \pm 101	382 \pm 56	246 \pm 66	472 \pm 59	0.54	0.02*
VEGFA (pg/ml)	7.5 \pm 1.3	7.7 \pm 1.8	10 \pm 0.2	6 \pm 2.9	0.55	0.11
IL20 (pg/ml)	233 \pm 72.7	206 \pm 73	210 \pm 189	204 \pm 75	0.55	0.35
IL33 (pg/ml)	87 \pm 61	67 \pm 23	110 \pm 65	46 \pm 13	0.55	0.50
TPO (pg/ml)	771 \pm 646	309 \pm 85	389 \pm 188	256 \pm 78	0.56	0.69
IL23 (ng/ml)	2.8 \pm 2.3	1.5 \pm 0.5	1.8 \pm 1	1.3 \pm 0.5	0.57	0.66
IL12p70 (pg/ml)	32 \pm 23	11 \pm 2.6	14 \pm 5.4	9.3 \pm 2.6	0.57	0.35
MMP1 (ng/ml)	0.9 \pm 0.2	1.2 \pm 0.3	0.5 \pm 0.2	1.5 \pm 0.3	0.57	0.06
TRAIL (pg/ml)	16 \pm 2.5	21 \pm 4.2	23 \pm 6.5	20 \pm 5.9	0.58	0.58
TIMP4 (pg/ml)	708 \pm 90	774 \pm 94	763 \pm 195	779 \pm 117	0.61	0.99
MIG/CXCL9 (ng/ml)	1.4 \pm 0.2	2.8 \pm 1.6	1.4 \pm 0.09	3.8 \pm 2.6	0.61	0.72
MMP12 (pg/ml)	634 \pm 49	599 \pm 29	556 \pm 16	618 \pm 40	0.64	0.44
IL17F (pg/ml)	65 \pm 38	93 \pm 52	165 \pm 113	35 \pm 12	0.64	0.21
IL17E/IL25 (ng/ml)	1 \pm 0.2	1.5 \pm 0.6	2.4 \pm 1.4	0.9 \pm 0.2	0.64	0.29
Eotaxin3 (pg/ml)	10 \pm 3.6	8 \pm 1.7	7.7 \pm 3.5	8.1 \pm 2.1	0.66	0.67
PDGFAA (ng/ml)	1.1 \pm 0.2	1.3 \pm 0.4	1.1 \pm 0.7	1.4 \pm 0.5	0.69	0.53
MMP13 (pg/ml)	393 \pm 76	394 \pm 106	37 \pm	454 \pm 103	0.71	0.01*
IL28A (pg/ml)	931 \pm 463	800 \pm 318	897 \pm 851	752 \pm 310	0.71	0.35
IL2 (pg/ml)	12 \pm 9	7.5 \pm 4.4	15 \pm 11	2.5 \pm 0.5	0.72	0.17
IL13 (pg/ml)	90 \pm 10	117 \pm 26	154 \pm 48	93 \pm 28	0.73	0.27
RANTES (ng/ml)	6.6 \pm 2.3	8.6 \pm 2.6	6.6 \pm 5.7	9.9 \pm 2.4	0.75	0.35
MMP9 (ng/ml)	255 \pm 59	249 \pm 71	80 \pm 25	321 \pm 88	0.76	0.04*
PDGFAB/BB (ng/ml)	12.3 \pm 2.1	15.9 \pm 3.5	11.4 \pm 7.1	18.9 \pm 3.5	0.76	0.14
ENA78 (pg/ml)	80 \pm 33	61 \pm 13	48 \pm 14	70 \pm 20	0.76	0.45
SCF (pg/ml)	15 \pm 5.5	19 \pm 7.2	26 \pm 15	15 \pm 8.5	0.79	0.36
MCP2 (pg/ml)	14 \pm 1.3	14 \pm 1.2	16 \pm 1.5	13 \pm 1.7	0.80	0.27
MCSF (pg/ml)	139 \pm 20	157 \pm 28	144 \pm 32	166 \pm 43	0.80	0.82
IFN α 2 (pg/ml)	191 \pm 91	183 \pm 67	263 \pm 171	129 \pm 14	0.80	0.68
GCSF (pg/ml)	46 \pm 6.6	45 \pm 7.1	51 \pm 12	41 \pm 9.2	0.81	0.47
MCP3 (pg/ml)	19 \pm 2.1	25 \pm 7.3	24 \pm 8.1	26 \pm 12	0.82	0.81
IL9 (pg/ml)	16 \pm 2.2	19 \pm 4.9	24 \pm 13	15 \pm 3	0.86	0.59
IL10 (pg/ml)	7.2 \pm 1.3	6.7 \pm 1	7.9 \pm 1.3	5.9 \pm 1.4	0.87	0.26
6CKine (pg/ml)	307 \pm 58	326 \pm 50	335 \pm 99	320 \pm 61	0.87	0.92

IL22 (pg/ml)	82±8.2	102±31	92±27	109±51	0.91	0.89
EGF (pg/ml)	42±7.9	44±10	59±17	30±6.7	0.93	0.21
IL7 (pg/ml)	24±23	4.7±1.7	7.8±3.3	2.2±0.6	0.94	0.37
MDC (ng/ml)	0.7±0.1	0.9±0.3	0.6±0.2	1.1±0.5	0.95	0.46
IL3 (pg/ml)	1.3±0.2	1.6±0.3	1.4±0.6	1.7±0.5	0.95	0.80
MIP1 α (pg/ml)	51±2.4	63±17	86±42	47±7.2	0.95	0.42
FGF2 (pg/ml)	233±93	205±49	286±93	151±49	0.96	0.20
BCA1 (pg/ml)	351±157	261±58	278±81	249±87	0.98	0.83
IL4 (pg/ml)	1.6±0.2	2.8±1	4.5±2.2	1.7±0.7	1.00	0.31

Table S5.

Group characteristics for human placental analyses (Control n=17, All PreE n=21, Preterm PreE=13, Term PreE n=8); Data represent mean \pm SEM. * $P < 0.05$ vs. control, one-way ANOVA with Bonferroni multiple comparisons procedure or Chi-square test. PreE, preeclampsia.

	Control	All PreE	Preterm PreE	Term PreE	<i>P</i> value
Gestational age at delivery (weeks)	38.5 \pm 0.3	35.2 \pm 0.5*	33.6 \pm 0.4*	37.7 \pm 0.3	<0.0001
% C section	47	81	77	88	0.16
Maternal age (years)	30.2 \pm 1.1	32.8 \pm 1.2	31.5 \pm 1.6	34.8 \pm 1.7	0.20
Maternal BMI	29.7 \pm 1.6	34.4 \pm 1.7	35.4 \pm 2.1	33.0 \pm 3.0	0.22
Peak systolic blood pressure (mmHg)	125 \pm 2	183 \pm 5*	185 \pm 7*	180 \pm 9*	<0.0001
Peak diastolic blood pressure (mmHg)	80 \pm 2	108 \pm 3*	109 \pm 3*	105 \pm 5*	<0.0001
Plasma creatine (mg/dL)	0.6 \pm 0.1	0.6 \pm 0.03	0.5 \pm 0.03	0.7 \pm 0.06	0.22
Lowest platelet count (x10 ⁹ /L)	209 \pm 11	208 \pm 16	207 \pm 24	209 \pm 18	0.99
AST (U/L)	17.8 \pm 1.5	55.2 \pm 25	59 \pm 38	47 \pm 18	0.90
ALT (U/L)	10.4 \pm 0.8	48.7 \pm 21	48 \pm 31	50 \pm 26	0.86

Table S6.

Group characteristics for human plasma analyses (Control n=10, All PreE n=10, “Non-Severe” PreE=4, Severe PreE n=6); Data represent mean \pm SEM. * $P < 0.05$ vs. control, one-way ANOVA with Bonferroni multiple comparisons procedure or Chi-square test. PreE, Preeclampsia.

	Control	All PreE	“Non-Severe” PreE	Severe PreE	P value
Gestational age at delivery (weeks)	38.8 \pm 0.3	35.5 \pm 1.0*	36.3 \pm 0.6	35.0 \pm 1.6*	0.02
% C section	50%	30%	25%	33%	0.75
Maternal age (years)	29.1 \pm 1.4	29.1 \pm 1.7	29.5 \pm 2.3	28.8 \pm 2.6	0.99
Maternal BMI	29.1 \pm 2.1	33.8 \pm 2.7	38.6 \pm 3.2	30.7 \pm 3.5	0.11
Peak systolic blood pressure (mmHg)	137 \pm 5	181 \pm 7*	169 \pm 10*	189 \pm 8*	<0.0001
Peak diastolic blood pressure (mmHg)	88 \pm 4	112 \pm 4*	103 \pm 5	119 \pm 3*	<0.0001
Plasma creatine (mg/dL)	0.6 \pm 0.1	1.0 \pm 0.2	1.1 \pm 0.5	0.9 \pm 0.2	0.58
Lowest platelet count (x10 ⁹ /L)	220 \pm 14	194 \pm 16	184 \pm 20	201 \pm 25	0.56
AST (U/L)	21.4 \pm 3.7	17.8 \pm 1.7	16.5 \pm 1.7	18.7 \pm 2.7	0.65
ALT (U/L)	16.0 \pm 2.7	14.0 \pm 1.8	10.3 \pm 2.0	16.5 \pm 2.3	0.34

Table S7.

Output from bulk RNA-sequencing of *hM3Dq^{F/F} dam x Gcm1-Cre^{+/-} sire placentas (n=6 per group, GD 14.5)*; Seq, sequence. GC, guanine and cystine. Dupl, duplication.

Alias	Seq Length R1/R2	GC (%) R1/R2	Dupl (%) R1/R2	Total Reads	Total Read Pairs	Mapped Read Pairs	Mapped Read Pairs (Junction)	Gene Counts	Exon Counts
Saline Cre-rep1	35-101	49	67/63	87,638,186	43,819,093	41,974,798	22,442,337	36,114,573	112,272,157
Saline Cre-rep2	35-101	49	68/64	90,452,812	45,226,406	43,994,392	23,114,472	37,605,219	121,998,114
Saline Cre-rep3	35-101	49	67/63	88,368,902	44,184,451	42,743,206	22,734,828	36,921,120	122,267,848
Saline Cre-rep4	35-101	49	64/62	70,243,630	35,121,815	34,217,114	18,633,457	29,546,183	95,748,048
Saline Cre-rep5	35-101	49	63/60	69,935,484	34,967,742	33,764,744	18,192,487	29,139,637	93,650,569
Saline Cre-rep6	35-101	49	62/59	67,581,876	33,790,938	32,870,475	17,384,342	28,010,106	91,132,626
CNO Cre-rep1	35-101	48/49	66/63	61,513,588	30,756,794	30,020,151	14,269,222	25,774,173	80,960,644
CNO Cre-rep2	35-101	49	65/61	71,451,946	35,725,973	34,493,138	18,285,867	29,941,725	96,152,912
CNO Cre-rep3	35-101	49	67/59	84,846,794	42,423,397	37,663,204	19,627,648	32,422,859	102,816,499
CNO Cre-rep4	35-101	49	66/63	84,847,524	42,423,762	41,245,979	22,553,785	35,723,300	117,801,295
CNO Cre-rep5	35-101	49	74/71	119,436,068	59,718,034	57,956,583	30,953,633	51,138,547	164,571,296
CNO Cre-rep6	35-101	49	68/65	85,132,310	42,566,155	41,057,787	22,865,916	35,724,483	113,677,027
CNO Cre+ rep1	35-101	48/49	67/63	68,283,476	34,141,738	32,944,901	16,650,781	28,603,016	92,073,254
CNO Cre+ rep2	35-101	48/49	68/65	99,058,938	49,529,469	48,267,349	26,054,168	42,117,438	137,398,378
CNO Cre+ rep3	35-101	49/50	65/62	86,620,780	43,310,390	41,831,187	22,274,345	36,058,066	117,081,731
CNO Cre+ rep4	35-101	49	65/62	74,323,926	37,161,963	36,139,306	19,735,665	31,324,080	101,610,178
CNO Cre+ rep5	35-101	49	70/67	104,004,496	52,002,248	50,628,243	27,883,522	44,305,274	145,035,566
CNO Cre+ rep6	35-101	49/50	66/61	75,679,152	37,839,576	36,172,091	19,342,315	31,286,573	101,188,637
CNO+MitoQ Cre+ rep1	35-101	49	66/63	71,566,736	35,783,368	34,820,675	19,488,162	30,386,501	98,857,519
CNO+MitoQ Cre+ rep2	35-101	49/50	64/61	68,279,128	34,139,564	33,041,796	17,340,770	28,424,137	92,740,972
CNO+MitoQ Cre+ rep3	35-101	49	67/63	86,721,048	43,360,524	42,204,749	22,449,771	36,285,408	113,285,493
CNO+MitoQ Cre+ rep4	35-101	49	65/62	64,509,404	32,254,702	31,348,040	16,539,275	27,112,272	87,626,226
CNO+MitoQ Cre+ rep5	35-101	49	68/65	74,821,202	37,410,601	36,311,340	19,992,334	32,278,701	106,355,824
CNO+MitoQ Cre+ rep6	35-101	49	67/64	77,040,634	38,520,317	37,339,523	20,129,837	32,556,419	104,454,720