Supplementary Experimental procedure

Tissue preparation, Histology and Immunohistochemistry

Embryos and placentae were harvested in ice cold 1x Phosphate buffered saline (PBS) from timed mating and fixed in 4% paraformaldehyde/PBS overnight at 4°C. Tissues were washed with PBS thrice and cut into two halves for paraffin and cryo embedding. For paraffin embedding, tissues were dehydrated through a graded ethanol series and embedded as paraffin blocks. 4 µm sections were cut and processed for histology and IHC. For cryo sections, tissues were incubated overnight at 4°C in 10% and 25% sucrose respectively followed by freezing in OCT in dry ice. Blocks were stored at -80°C and 10 µm sections were cut on Superfrost slides for in situ hybridization (ISH). Histological sections were stained with Hematoxylin and Eosin (H/E) using standard protocol. IHC was performed as published previously (Kuckenberg et al., 2010). 4 µm hydrated deparaffinized paraffin sections following antigen retrieval were incubated with primary antibody against Tfap2c (1:250; sc53162-6E4/4, Santa Cruz), Ki-67(1:250; TEC-3, DAKO, Germany), CD-31(1:20; SZ31, Dianova, Germany), pERK1/2(1:50, #4370 cell signaling), and pAKT(1:50,# 4060, cell signaling) overnight at 4 °C. Anti-rabbit (1:500; DAKO, Hamburg, Germany) and anti-rat (1:200; DAKO) secondary antibodies were used for 30 minutes at room temperature. Signals were visualized using a Vectastain ABC kit (Vector Laboratories, Germany). Sections were photographed using Diskus software (Hilden, Germany).

ISH

Briefly, sections were rehydrated in 1x PBS, fixed in 4% PFA and incubated with 30µg/ml Proteinase K for 10 minutes at 37°C. Each step was followed by careful washing with PBS for 5 minutes each. Sections were hybridized overnight with DIG labeled probes (2ng/µl) at 65°C. Following day, sections were washed, incubated with RNaseA and subsequently blocked for an hour at room temperature, incubated with anti-DIG antibody conjugated to alkaline phosphatase (1:2000; Roche, Mannheim, Germany) at 4°C overnight. Sections were washed, developed and counter stained with NuclearFastRed (Sigma, Germany) and mounted with Entellan (Merck, Germany).

TUNEL

Cryo sections were fixed in 4%PFA for 15 minutes and incubated with 20 µg/ml of proteinase K for 15 minutes and washed with PBS. For positive control, sections were treated with DNAse 1 for 15 minutes and rinsed with PBS The sections were incubated with equilibration buffer for 5–10 minutes following incubation with rTdT (Terminal Deoxynucleotidyl Transferase, Recombinant) reaction mix including rTdT enzyme and biotinylated nucleotide mix in a humidified atmosphere at 37 °C for 1 hour. The sections were further washed with 2× SSC for 15 minutes at room temperature. The endogenous peroxidase activity was blocked with 0.3% hydrogenperoxide followed by subsequent washing step in PBS thrice for 5 minutes each. The sections were then incubated with Streptavidin HRP for 30 minutes and staining was done with diaminobenzidine followed by washing and mounting the sections.

Laser microdissection

10 µm sections were cut with a cryomicrotome (Leica CM 1850 UV, Germany) and collected on membrane coated glass slides (Membrane Slides 1.0 PEN, Zeiss, Germany). The samples were fixed at -20° C with Ethanol and stained with Cresyl violet (Merck, Germany) according to the manufacturer's instructions. For preservation and improving the visualization of the tissue under the microscope, the sections were mounted with Liquid Cover Glass (Zeiss, Germany). Laser Microdissection was performed with the PALM MicroBeam System (Zeiss, Germany) with an Axiovert microscope (Zeiss, Germany). The software used was PALM RoboSoftware 4.2 (Zeiss, Germany).

Western Blot

For protein analysis, 25 µg of protein was run on a 10% SDS-PAGE and transferred onto a nitrocellulose membrane. Primary antibodies were used to detect TFAP2C (1:500, 6E4/4 sc-53162, Santa Cruz), pERK1/2 (1:1000, #4370, cell signaling), ERK1/2 (1:1000, #9102, cell signaling), pP38 (1:1000, #9211, cell signaling,, P38 (1:1000, #9212, cell signaling), pAKT (1:1000, #4060, cell signaling), AKT (1:1000, #4691, cell signaling) and B-ACTIN (1:50000; AC-15, Sigma Aldrich).

HRP conjugated secondary antibodies were used (anti-mouse 1:1000; anti rabbit 1:2000, DAKO) and the membrane was incubated with Pierce- Super Signal West Pico chemiluminescent substrate (Thermo scientific) and the signal was detected using ChemiDoc MP imaging system (BIO-RAD).

Softwares:

Web based GeneMANIA (Warde-Farley et al., 2010) (www.genemania.org), String (Jensen et al., 2009) (www.string-db.org) and rVista algorithm (Loots and Ovcharenko, 2004) softwares were used.

Supplementary figures

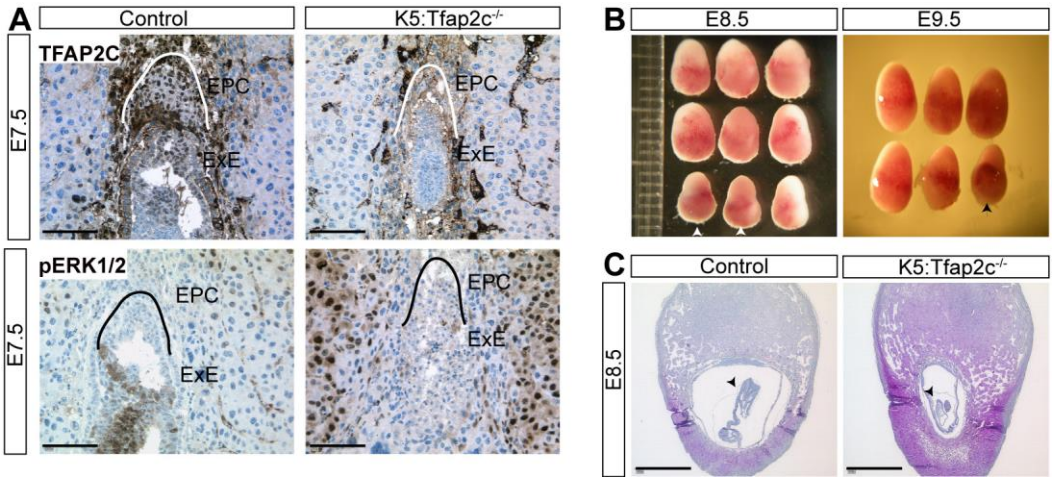

Fig. S1: Smaller implantation in K5Cre:Tfap2c$^{-/-}$ placentae. (A) IHC against TFAP2C and pERK1/2 at E7.5 placental sections of K5Cre:Tfap2c$^{-/-}$ and control. Scale bar- 100µm (B) Whole implantation isolated from K5Cre:Tfap2c$^{-/-}$ E8.5 and E9.5 respectively. Arrowheads show smaller K5Cre:Tfap2c$^{-/-}$ implantation. (C) H/E stained placentae of control and K5Cre:Tfap2c$^{-/-}$ at E8.5. Arrowheads indicate smaller embryo in K5Cre:Tfap2c$^{-/-}$. Scale bar 1000µm.

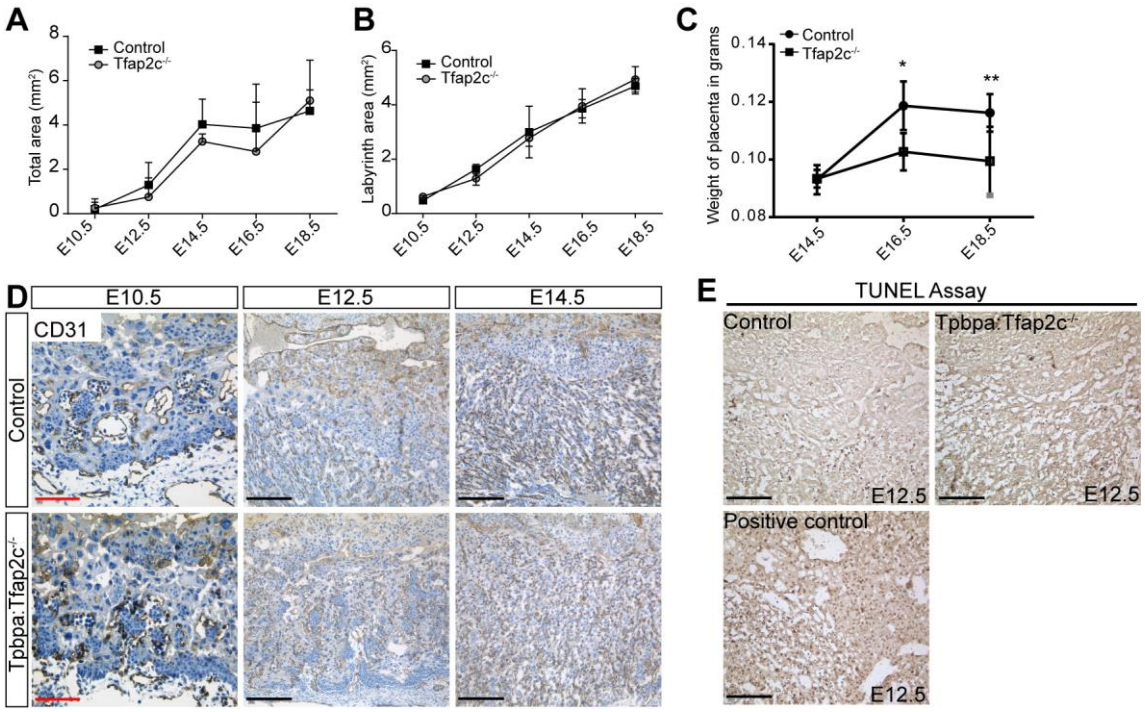

Fig. S2: Analysis of Tpbpa:Tfap2c$^{-/-}$ placentae. (A) Total area of the control and Tpbpa:Tfap2c$^{-/-}$ placentae at E10.5 (n=2 each), E12.5 (n=3 each), E14.5 (n=6 each), E16.5 (n=4 each) and E18.5 (n=6 each). (B) Labyrinth area of the control and Tpbpa:Tfap2c$^{-/-}$ placentae at E10.5 (n=2 each), E12.5 (n=3 each), E14.5 (n=6 each), E16.5 (n=4 each) and E18.5 (n=6 each). (C) Weight of Tpbpa:Tfap2c$^{-/-}$ and control placentae show lighter Tpbpa:Tfap2c$^{-/-}$ placenta at E16.5 (n=11 control, n=3 mutant) and E18.5 (n=13 control, n=7 mutant). (D) IHC against CD-31 on paraffin embedded sections at E10.5, E12.5 and E14.5 respectively in control and Tpbpa:Tfap2c$^{-/-}$ placentae. (E) TUNEL staining to detect apoptotic cells on cryo embedded E12.5 control and Tpbpa:Tfap2c$^{-/-}$ placentae with positive control. Black scale bar- 200 µm, Red scale bar- 100 µm. Data are represented as mean +/- SD. ** $p \leq 0.005$,* $p \leq 0.05$

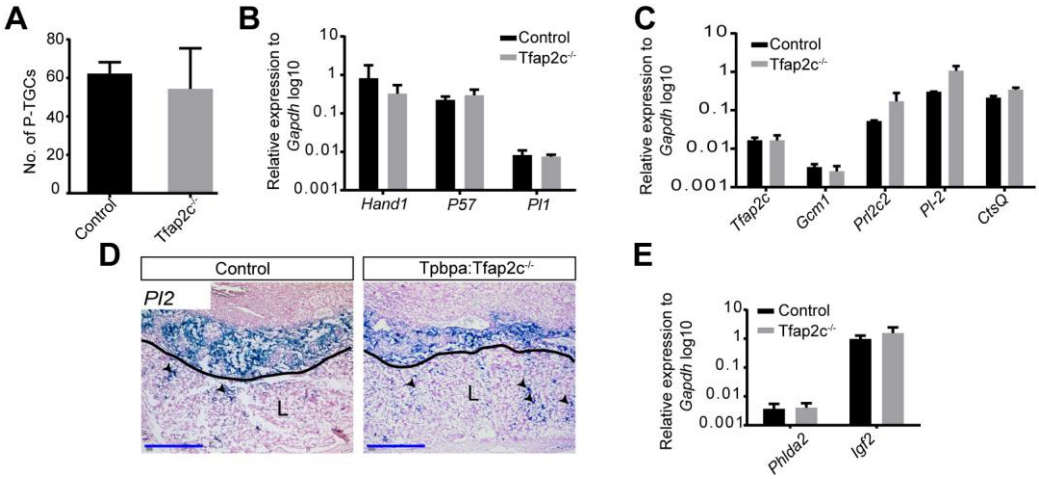

Fig. S3: Analysis of JZ and labyrinth of Tpbpa:Tfap2c$^{-/-}$ placentae. (A) Quantification of P-TGCs on E12.5 Tpbpa:Tfap2c$^{-/-}$ and control placentae by counting the number of P-TGCs on 3 different sections each. (B) Samples were obtained by laser microdissection of SpT from E14.5 Tpbpa:Tfap2c$^{-/-}$ and control placentae (n=4 each) and expression levels relative to *Gapdh* in log10 scale were measured. *Hand1*, *p57 and Pl1* did not show any deregulation compared to the control placentae. (C) Samples were obtained by laser microdissection of Labyrinth from E14.5 Tpbpa:Tfap2c$^{-/-}$ and control placentae (n=2 Tpbpa:Tfap2c$^{-/-}$ and n=3 control) and expression levels (relative to *Gapdh*, log10 scale) of *Tfap2c, Gcm1, Prl2c2, Pl2* and *CtsQ* were measured. Increased expression of *Prl2c2* and *Pl2* is detected. (D) In situ hybridization on cryo embedded sections at E14.5 against *Pl2*. Arrows show increased number of *Pl2* positive cells in the labyrinth of Tpbpa:Tfap2c$^{-/-}$ placentae compared to the control. (E) Samples were obtained by laser microdissection of JZ from E14.5 Tpbpa:Tfap2c$^{-/-}$ and control placentae (n=3 each) and expression levels (relative to *Gapdh*, log10 scale) of *Phlda2* and *Igf2* were measured. L- labyrinth, Blue scale bar- 500 µm. Data are represented as mean +/- SD.

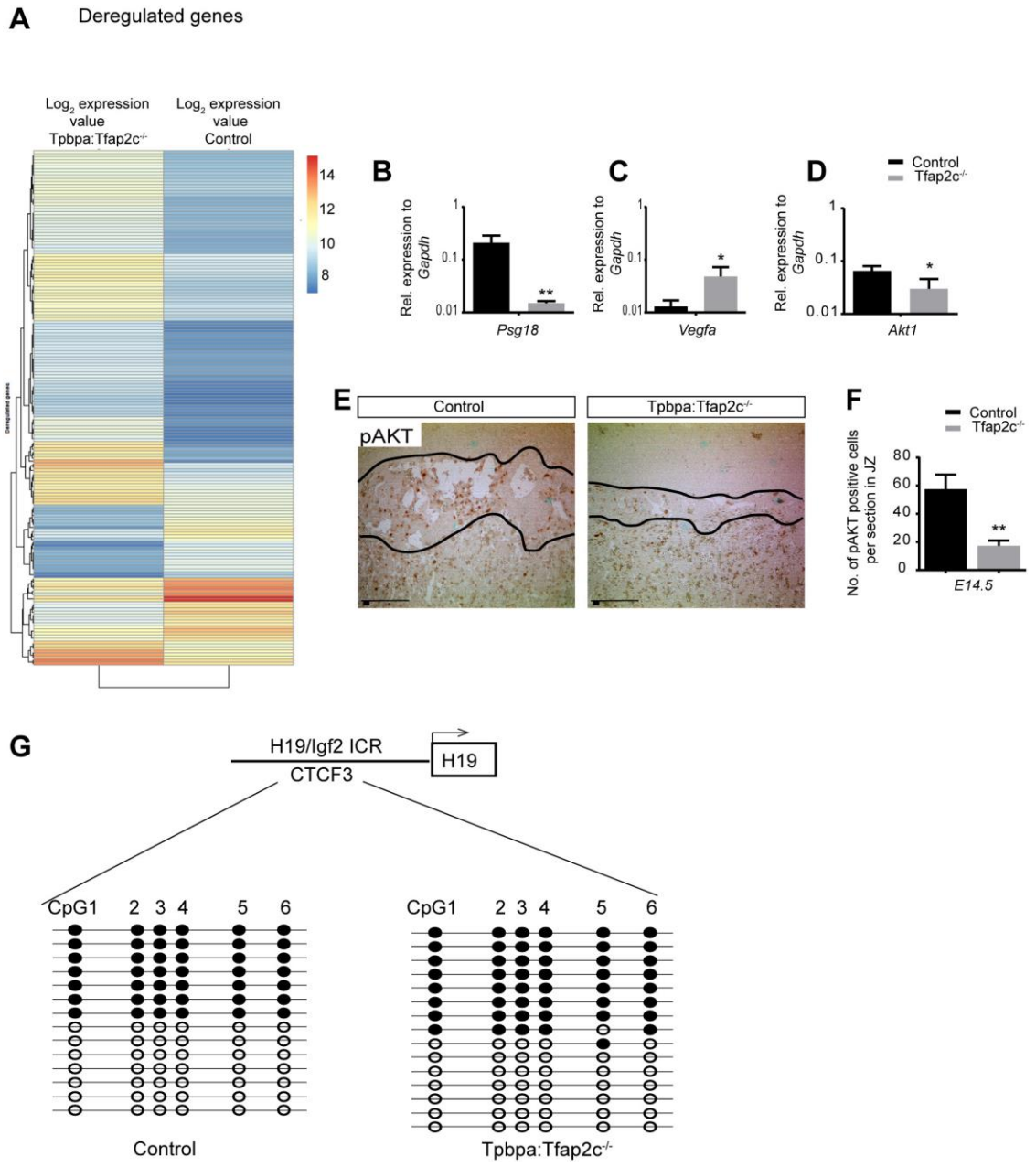

Fig. S4: Validation of genes deregulated in the microarray analysis of laser microdissected JZ from control and Tpbpa:Tfap2c$^{-/-}$ placentae at E14.5. (A) Heat map showing expression values of all deregulated genes in Log_2 scale in control and Tpbpa:Tfap2c$^{-/-}$ placentae. Log-transformed expression values are presented on a scale of 8 to 14. Upregulated genes are indicated in shades of red; downregulated in blue. (B) Samples were obtained by laser microdissection of SpT from E14.5 Tpbpa:Tfap2c$^{-/-}$ and control placentae (n=4 each) and expression levels relative to *Gapdh* were measured by qRT-PCR. Note significant downregulation of *Psg18*, (C) *Vegfa* and (D) *Akt1*. (E) IHC against pAKT on placental sections E14.5. (F) Quantification of pAKT positive cells.Three different high magnification areas were counted each. Data are represented as mean +/- SD. ** $p \leq 0.005$,* $p \leq 0.05$. (G) Graphical representation of % methylation of CTCF3 region in H19 ICR domain in JZ of Tpbpa:Tfap2c$^{-/-}$ (n=15) and control placentae (n=16).

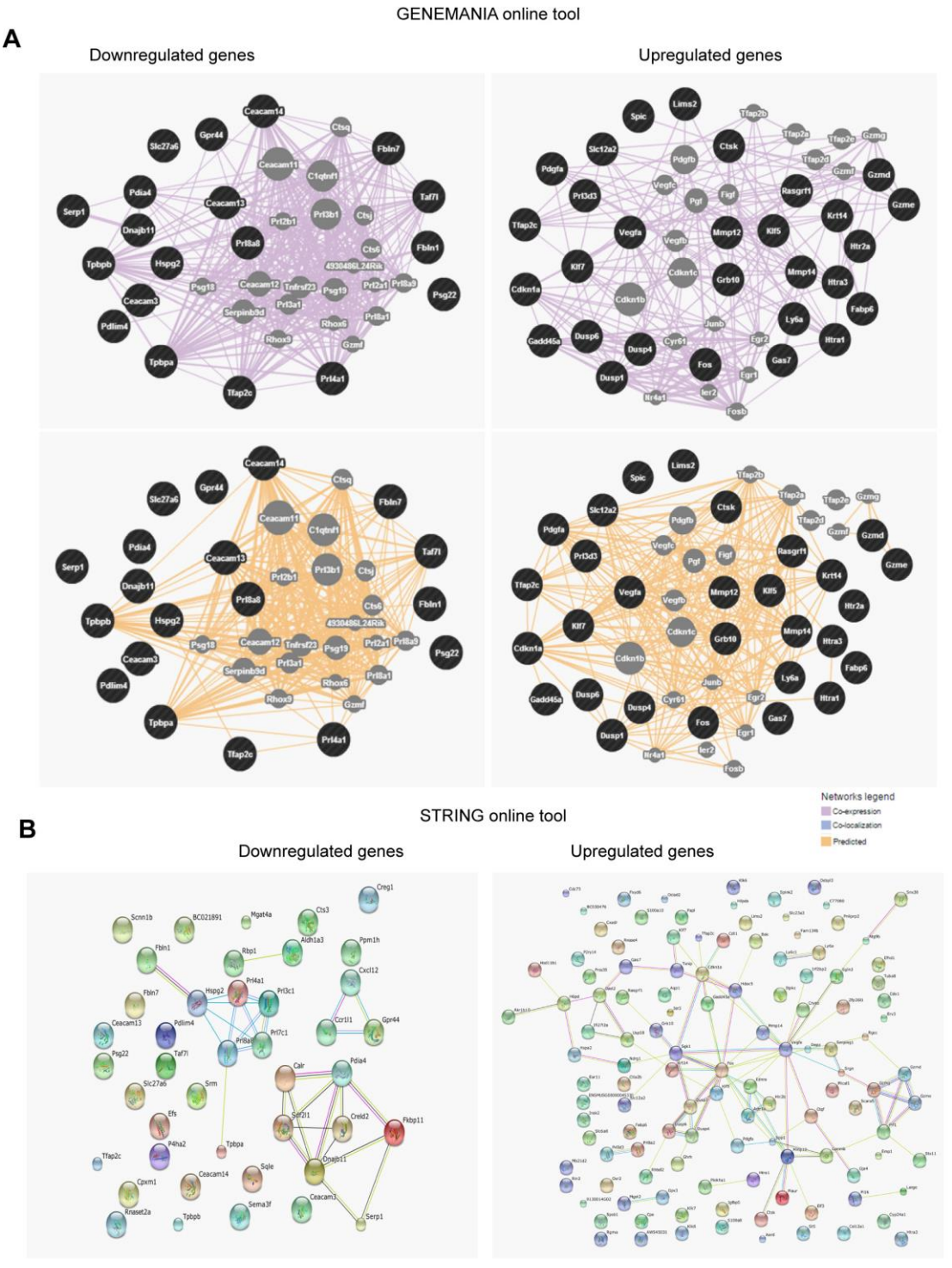

Fig. S5: Interactive analysis of deregulated genes from expression microarray data. (A) Interactive gene network analysis of up and downregulated genes using GENEMANIA online tool. Note linked co-expression of Tfap2c and Tpbpa in downregulated genes. Purple lines indicate co-expression and orange lines indicate predicted interaction among the genes. (B) Interactive known and predicted protein- protein association using STRING online tool.

Table S1: List of upregulated genes in the JZ of mutant placentae at E13.5
Table S2: List of downregulated genes in the JZ of mutant placentae at E13.5
Table S3: GO grouping of differentially regulated genes identified in murine placental JZ microarray analysis
Table S4: Deregulated genes with fold change and p value in qRT-PCR relative to the control
Table S5: Sequence of genotyping primers
Table S6: Gene name and sequences of primers used for quantitative RT- PCR and ChIP and Bisulfite sequencing
Table S7: shRNA oligonucleotide sequence

Table S1: List of genes upregulated in the JZ of mutant placentae

Gene symbol	FC>1.5 (Log2
Osbpl3	**1.509086**
C77080	1.523591
H6pd	1.526885
Prl3d3	1.528163
Snx30	1.531885
Slc6a8	1.537295
Grb10	1.542198
Slc12a2	1.554466
Sgk1	1.565943
Plaur	1.567605
Rhbdl2	1.575135
Mmp14	1.575289
Ly6c1	1.578245
4933402E13Rik	1.578724
LOC385615	1.58095
Rasgrf1	1.588314
Atg9b	1.589724
Gzmd	1.594451
Cdt1	1.595864
4732462B05Rik	1.596131
Ndrg1	1.599179
Rnase4	1.602184
Hspa2	1.60634
Cdo1	1.607689
Plekha1	1.608894
Oasl2	1.612556
Irak2	1.615824
Cxadr	1.624538
Prf1	1.657681
2310005E10Rik	1.657707
Gadd45a	1.670023
Irf2bp2	1.676604

Irak2	1.67875
Aqp1	1.705648
Cdc73	1.706444
Egln3	1.707686
Elf3	1.711483
Tuba8	1.721988
Htr2b	1.725925
Cyp24a1	1.72717
Usp18	1.72859
2310016C08Rik	1.734629
Large	1.740121
Prl3d3	1.740349
Cdkn1a	1.741578
Spsb1	1.743703
Ociad2	1.746128
St5	1.747912
Itpkc	1.751357
1600021P15Rik	1.773339
Ndrl	1.775981
Klf5	1.782944
Klf7	1.783327
Gzme	1.784651
Mical1	1.785555
1600014E20Rik	1.789272
Fxyd6	1.790198
BC030476	1.790865
Serping1	1.798993
Srgn	1.807363
Gzmd	1.825638
St5	1.839717
B230343A10Rik	1.84686
Dusp4	1.84861
Dusp6	1.860065
Rasgrf1	1.870452
Gpnmb	1.87048
Ctgf	1.873728
Aard	1.893147
Bok	1.898854
Spp1	1.904676
Klk7	1.9048
Osr2	1.905259
Stx11	1.914442
Klf7	1.915583
Zfp36l1	1.918171
Prss35	1.924599
S100a10	1.931051

Ghrh	1.937728
Hsd11b1	1.938285
Hsd11b1	1.95428
P2ry14	1.955215
Cpe	1.96212
C330005M16Rik	1.968196
Osbpl3	1.969108
Cryab	1.970954
Txnip	1.975591
Hdac5	1.986672
Ly6a	1.991316
Slc23a3	1.998663
S100a8	2.016638
Hsd11b1	2.021868
Gas7	2.026153
Fabp6	2.048584
Lims2	2.066802
Klf7	2.068018
Txnip	2.088046
Ier3	2.090304
Pi16	2.099015
Ear11	2.104489
Ctgf	2.116343
Dusp1	2.116575
Htra1	2.117235
Vegfa	2.124982
Klk6	2.130946
Scara5	2.135991
Mgst2	2.147432
Ctsk	2.156731
Mmp12	2.160021
Rgma	2.161246
Efhd1	2.180658
Prl3d3	2.183273
Pdgfa	2.187754
Gpx3	2.191067
Rin2	2.23222
4930486L24Rik	2.254293
Htra3	2.256029
Gzmg	2.275722
Pnliprp2	2.285754
Prl8a2	2.363383
Htra1	2.425347
scl0001849.1_2273	2.436885
Dusp4	2.460281
Krt14	2.473251

Lims2	2.612874
8430408G22Rik	2.622677
Gas7	2.630254
Igfbp5	2.639024
Prss18	2.656949
Agtr1a	2.661501
Lims2	2.697922
Ednra	2.761526
4930539E08Rik	3.055416
Gja4	3.132141
Col12a1	3.140382
Fos	3.192744
Ctla2b	3.2266
Pnliprp2	3.275906
Igfbp5	3.32744
1190002H23Rik	3.392156
Igfbp5	3.461613
Fam134b	3.552477
Ifi27	4.147568
Emp1	4.181227
Klk8	4.650642
Spink2	5.626195

Table S2: List of genes downregulated in the JZ of mutant placentae

Gene symbol	FC>1.5 (Log2)
eGFP	**-3.77727**
Cts3	-3.7038
LOC381852	-3.06463
Prlpc3	-2.88441
Creg1	-2.73667
Ceacam13	-2.68573
Fkbp11	-2.58183
Ceacam14	-2.52696
Ceacam13	-2.41975
Creld2	-2.37883
Calr	-2.35118
Sdf2l1	-2.32642
BC021891	-2.28505
Sema3f	-2.27968
Ceacam3	-2.23943
Fbln7	-2.22116
Creld2	-2.20439
P4ha2	-2.18194
Scnn1b	-2.17906
Cxcl12	-2.17149
Prl4a1	-2.16109
C030002B11Rik	-2.13341
Sema3f	-2.10653
Psg22	-2.08036
Pdia4	-2.02606
Ceacam14	-2.00069
Prl3c1	-1.97935
Aldh1a3	-1.94388
Prl7c1	-1.94014
P4ha2	-1.92095
Tpbpb	-1.90947
Dnajb11	-1.86672
Pdlim4	-1.85605
Efs	-1.84588
Ccr1l1	-1.80664
9530018I07Rik	-1.7933
Rbp1	-1.67397
Fbln1	-1.66694
Tpbpa	-1.653
Fbln1	-1.63775
Hspg2	-1.63722
Gpr44	-1.61621
Slc27a6	-1.59768

LOC100044439	-1.59259
Sqle	-1.57135
Srm	-1.57097
scl0001259.1_60	-1.55067
Cpxm1	-1.53658
Rnaset2	-1.52336
Taf7l	-1.5066
D3Ucla1	-1.50564

Table S3: GO grouping of differentially regulated genes identified in murine placental JZ microarray analysis

#	Category	GO Reference	Expected	observed	False Discovery Rate (p-value)	Sub-Category
1	**Gene Ontology**	GO:0005576	8.39952	42	5.62151e-17	extracellular region
2	**Gene Ontology**	GO:0008152	36.408	76	5.44931e-11	metabolic process
3	**Gene Ontology**	GO:0048731	11.5921	39	1.38595e-10	system development
4	**Gene Ontology**	GO:0009987	57.2054	98	1.54034e-10	cellular process
5	**Gene Ontology**	GO:0005488	51.9179	91	4.0732e-10	binding
6	**Gene Ontology**	GO:0048856	12.9115	40	4.0732e-10	anatomical structure development
7	**Gene Ontology**	GO:0065008	7.4226	30	4.0732e-10	regulation of biological quality
8	**Gene Ontology**	GO:0050896	13.3899	40	9.8153e-10	response to stimulus
9	**Gene Ontology**	GO:0005515	27.097	59	3.65362e-09	protein binding
10	**Gene Ontology**	GO:0007275	14.1754	40	4.22509e-09	multicellular organismal development
11	**Gene Ontology**	GO:0044238	31.5083	64	6.63305e-09	primary metabolic process
12	**Gene Ontology**	GO:0048513	9.15991	30	2.55178e-08	organ development
13	**Gene Ontology**	GO:0032502	15.389	40	3.41949e-08	developmental process
14	**Gene Ontology**	GO:0065007	35.7181	66	1.2802e-07	biological regulation
15	**Gene Ontology**	GO:0019538	11.9749	33	2.06102e-07	protein metabolic process
16	**Gene Ontology**	GO:0003824	24.6295	51	2.65436e-07	catalytic activity
17	**Gene Ontology**	GO:0043170	25.3748	52	2.65436e-07	macromolecule metabolic process
18	**Gene Ontology**	GO:0005737	34.3031	63	3.27729e-07	cytoplasm
19	**Gene Ontology**	GO:0005623	72.7908	102	2.38784e-06	cell
20	**Gene Ontology**	GO:0044464	72.7858	102	2.38784e-06	cell part
21	**Gene Ontology**	GO:0044237	30.7328	56	2.89122e-06	cellular metabolic process
22	**Gene Ontology**	GO:0044424	49.108	76	7.79736e-06	intracellular part
23	**Gene Ontology**	GO:0005622	50.2914	77	8.59119e-06	intracellular
24	**Gene Ontology**	GO:0050789	33.5679	58	8.59119e-06	regulation of biological process

25	**Gene Ontology**	GO:0050794	31.9615	56	8.59119e-06	regulation of cellular process
26	**Gene Ontology**	GO:0032501	24.1763	46	1.03389e-05	multicellular organismal process
27	**Gene Ontology**	GO:0031323	13.8381	31	2.33533e-05	regulation of cellular metabolic process
28	**Gene Ontology**	GO:0044444	21.2657	41	2.72158e-05	cytoplasmic part
29	**Gene Ontology**	GO:0019222	14.7697	32	3.00647e-05	regulation of metabolic process
30	**Gene Ontology**	GO:0043226	41.9472	62	0.000397499	organelle
31	**Gene Ontology**	GO:0043231	36.9065	56	0.000469096	intracellular membrane-bounded organelle
32	**Gene Ontology**	GO:0043227	36.967	56	0.00047478	membrane-bounded organelle
33	**Gene Ontology**	GO:0043229	41.8264	60	0.0011161	intracellular organelle
34	**Gene Ontology**	GO:0044260	22.3685	36	0.00267099	cellular macromolecule metabolic process
35	**Gene Ontology**	GO:0023052	20.6463	31	0.0148365	signaling
36	**Gene Ontology**	GO:0005575	147.822	143	0.0169492	cellular_component
37	**Gene Ontology**	GO:0016020	37.3245	49	0.0214605	membrane
38	**KEGG**	-	1.57107	8	0.000247678	MAPK signaling pathway

Table S4: Deregulated genes with p value in qRT-PCR related to Fig. 4C

Gene	Deregulated in Tpbpa:Tfap2c$^{-/-}$ placentae	Mean fold change	p-value
Prl8a8	Down	181.18	<0.0001
Prl3a1	Down	20.74	0.022
Tpbpa	Down	20.49	0.0025
Pcdh12	Down	4.69	0.0019
Gjb3	Down	4.23	0.00016
Pl1	Unchanged	1.06	ns
Pl2	Down	3.36	0.004
Prl2c2	Down	3.04	0.011
Rgs5	Down	4.58	0.003
Pcsk6	Down	2.76	0.024
Tle3	Unchanged	1.3	ns
CtsQ	Unchanged	1.25	ns
P21	Up	3.34	0.00018
H19	Up	2.11	0.03
Tex 19.1	Down	2.22	0.03
Ascl2	Down	8.19	0.00054
Slc38a4	Down	2.61	<0.0001

Table S5: List of genotyping primers

Primers	Sequence 5'-3'
Cre F	TAAAGATATCTCACGTACTGACGGTG
Cre R	TCTCTGACCAGAGTCATCCTTAGC
Tfap2c P1	AACAGGTTATCATTTGGTTGGGATT
Tfap2c P2	CAATTTTGTCCAACTTCTCCCTCAA
Tfap2c P3	AATAGTCAGCCACCGCTTTACTAGG

Table S6: Primer Sequences for quantitative RT-PCR, ChIP and bisulfate sequencing.

Target name	Sequence 5'-3'	Reference
Tfap2c	F: CCTGCTCAGCTCCACGTC R: CCTCCATTTTTGGACTTTGC	
Tpbpa	F: CCAGCACAGCTTTGGACATCA R: AGCATCCAACTGCGCTTCA	
Hand1	F: CCCCTCTTCCGTCCTCTTAC R: CTGCGAGTGGTCACACTGAT	
Ascl2	F: GGTGACTCCTGGTGGACCTA R: TCCGGAAGATGGAAGATGTC	
Pl1	F: TGGAGCCTACATTGTGGTGG R: TGGCAGTTGGTTTGGAGGA	
Pl2	F: CCAACGTGTGATTGTGGTGT R: TGCCACCATGTGTTTCAGAG	
Prl2c2	F: TGCTCCTGGATACTGCTCCTA R: GGCTTGTTCCTTGTTTTCTGG	
Gcm1	F:CCATGTGAAACTGCCTCAGA R: CTTCCTCTGTGGAGCAGTCC	
Pcdh12	F: CTCCTGTCCAGCAAATCTCC R: TCTGCTTGACCACTAGGCTTG	
Gjb3	F: CTCCTCTGCTGTGGGTCTTG R: ATGCCGTGGAGTACTGGTTC	
P21	F: CCGTTGTCTCTTCGGTCCC R: CATGAGCGCATCGCAATC	(Choi et al., 2012)
Prl3a1	AGAGCGAAAGTGCATGTGTG GCACCTCTGTTTCCCTTCAG	(Reichmann et al., 2013)
Prl8a8	AAATTATGTGGGTGCCTGGA TCACGCAGAATTTGTCTGTTG	(Reichmann et al., 2013)
Rgs5	F: AGGCCCCTAAAGAGGTGAAC R: GACGGTTCCACCAGGTTCTT	(Mould et al., 2012)
Pcsk6	F: CCCAGGCAGAGACTCCAGAA R: GGCACACACTGGTCTGTAAAGT	(Mould et al., 2012)
Tle3	F: TGGTGAGCTTTGGAGCTGTT R: CGGTTTCCCTCCAGGAAT	(Villanueva et al., 2011)
CtsQ	F: GAGGCAGTAGTGGTCATCCC R: CAGTACTTCTTCCTCCGGACT	
H19	F: GAAATGGTGCTACCCAGCTCAT R:TTCAGCTTCACCTTGGAGCAG	(Sferruzzi-Perri et al., 2009)
Tex19.1	AAAATGGGCCACCCACATCTC CCACTGGCCCTTGGACCAGAC	(Reichmann et al., 2013)
Slc38a4	F: TGATTGGGATGTTAGTCTGAGG R: GGCCTGGGTTAAAATGTGTG	
Psg18	TGCAGGCAAACATTTCAGAG GAGTATGACAGGGGCCTCAA	(Reichmann et al., 2013)
Vefga	F: GCACATAGAGAGAATGAGCTTCC R: CTCCGCTCTGAACAAGGCT	(Jo et al., 2010)
Akt1	F: TCGTGTGGCAGGATGTGTAT R: ACCTGGTGTCAGTCTCAGAGG	
Dusp1	F: CATCCCTGTGGAGGACAACC R: CAGCATCCTTGATGGAGTCTATG	
Dusp4	F: TGCTTAAAGGTGGCTATGAGAGG	

	R: CTCATTGGTGCTGGGAGGTA	
Dusp6	F: CGAGAATAGCAGCGACTGGA R: TGAAGCCACCTTCCAGGTAGA	
B-Actin	F: TGTTACCAACTGGGACGACA R: GGGGTGTTGAAGGTCTCAAA	
Gapdh	F: ACCACAGTCCATGCCATCAC R: TCCACCACCCTGTTGCTGTA	
mouseChIP p21	F: TACGGGTGCCGTACATCAG R:AGCCTGGTCACCTTCCTACA	(Schemmer et al., 2013)
mouseChIP Dusp6	F: GCTGCAGCCTAGAAAGGATAG R: GCGGGAACTCAAGCGTAAA	
Human-TFAP2C	F: GGCCCAGCAACTGTGTAAAGA R: GCAGTTCTGTATGTTCGTCTCCAA	(Schemmer et al., 2013)
Human-DUSP1	F: GTACATCAAGTCCATCTGAC R: GGTTCTTCTAGGAGTAGACA	
Human-DUSP4	F: TGGCAATAAGGACTCGGAATA R:GGATCTGTGGGTTTCATCACT	
Bisulfite H19 CTCF3	F: GGGTTTTTTTGGTTATTGAATTTTAA R: AATACACACATCTTACCACCCCTATA	(Fauque et al., 2010)

Table S7: shRNA oligonucleotide sequence

Primer	Sequence
shRNA1 3'UTR	5´GATCCCCGGGAAGAGTTTGTTACCTATTCAAGAGATAGGTAACAAACTCT TCCCTTTTTA 3´GGGCCCTTCTCAAACAATGGATAAGTTCTCTATCCATTGTTTGAGAAGGG AAAAATTCGA
shRNA 2 ORF	5´GATCCCCCAGAAGAGCCAAATCGAAATTCAAGAGATTTCGATTTGGCTCT TCTGTTTTTA´ 3´GGGGTCTTCTCGGTTTAGCTTTAAGTTCTCTAAAGCTAAACCGAGAAGAC AAAAATTCGA

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