Supplementary Information

Additional mitochondrial DNA influences the interactions between the nuclear and mitochondrial genomes in a bovine embryo model of nuclear transfer.

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Supplementary Table 1. List of the top ten most significant differentially expressed genes.

Top ten DEGs	Fold change	Regulation	FDR
Comparison between miNT and SCNT blastocysts derived from depleted cells			
XIST	4.910942736	Down	0.0044
TMEM41B	7.140375772	Down	0.0105
RPL23A	20.11221399	Down	0.0105
RPL17	6.502524816	Down	0.0105
BSG	5.555820543	Up	0.0105
ARF4	5.176582618	Down	0.0105
CEP135	5.582843056	Down	0.0108
TPT1	9.272767615	Down	0.0109
ZDHHC6	4.688089135	Down	0.0109
RAP1A	7.490177979	Down	0.0109
Comparison between miNT blastocysts derived from depleted cells cultured in the absence of TSA and SCNT blastocysts derived from depleted cells cultured in the presence of TSA			
PNRC2	6.759891075	Down	0.00265
BSG	6.639156685	Up	0.00265
XIST	4.462957289	Down	0.00265
AMD1	7.356400369	Down	0.00265
PAPOLA	4.011105744	Down	0.00265
TMEM41B	6.89714836	Down	0.00265
CEP135	6.130479841	Down	0.00265
RPL23A	21.30322581	Down	0.00265
FLNB	6.802193281	Up	0.00374
LARP4	4.453686473	Down	0.00374
Comparison between miNT blastocysts derived from depleted cells cultured in the presence of TSA and SCNT blastocysts derived from depleted cells cultured in the presence of TSA			
REEP3	7.851672511	Down	0.00285
RPL23A	11.6237204	Down	0.00285
TMEM41B	5.073565597	Down	0.00531
SSB	5.296355642	Down	0.00531
MOSPD1	5.256126509	Down	0.00531
RAN	10.68118643	Down	0.00531
SDCBP	3.858392738	Down	0.00642
JMJD1C	5.344296314	Down	0.00642
LOC782101	5.084126757	Down	0.00642
NEMF	4.355988061	Down	0.00649

Supplementary Table 2. List of the biological functions.

Categories	Functions annotation	p-Value	Predicted State	Activation z-score	No. of genes
Comparison between miNT and SCNT blastocysts derived from depleted cells					
Cell Cycle, Cell Morphology	formation of spindle apparatus	0.000662	Increased	2	8
	formation of mitotic spindle	0.00171	Increased	2	7
Cell Cycle, DNA Replication, Recombination, and Repair	recombination of cells	0.000000203	Increased	2.514	14
	homologous recombination of cells	0.00000047	Increased	2.514	13
	homologous recombination	0.000000716	Increased	2.177	15
Organismal Survival	organismal death	3.03E-11	Increased	2.177	140
Cell Death and Survival	cell viability	0.000000326	Decreased	-2.295	74
	cell survival	0.000000407	Decreased	-2.206	76
Cellular Movement	cell movement	0.00003	Decreased	-2.136	101
DNA Replication, Recombination, and Repair	metabolism of DNA	0.00000529	Decreased	-2.426	28
	DNA replication	0.0000418	Decreased	-2.062	19
Post-Translational Modification	ubiquitination of protein	0.0000377	Decreased	-2.164	23
Protein Synthesis	translation	0.0000873	Decreased	-2.085	18
Comparison between miNT blastocysts derived from depleted cells cultured in the absence of TSA and SCNT blastocysts derived from depleted cells cultured in the presence of TSA					
Cell Cycle, Cellular Assembly and Organization, DNA Replication, Recombination, and Repair	segregation of chromosomes	0.000335	Increased	2.218	15

Cell Cycle, DNA Replication, Recombination, and Repair	homologous recombination	0.000426	Increased	2.177	15
	recombination of cells	0.000109	Increased	2.514	14
	homologous recombination of cells	0.000165	Increased	2.514	13
Cellular Compromise, Cellular Function and Maintenance	endoplasmic reticulum stress response	0.00157	Increased	2.213	16
Cellular Assembly and Organization	formation of cytoplasmic aggregates	0.000097	Decreased	-2.578	8
Organismal Survival	organismal death	1.36E-18	Decreased	-2.187	243
	morbidity or mortality	3.88E-18	Decreased	-2.158	244
Protein Synthesis	modification of peptide	0.0000965	Decreased	-2.236	15
miNT blastocysts derived from depleted cells cultured in the presence of TSA and SCNT blastocysts derived from depleted cells cultured in the presence of TSA					
Cell Death and Survival	apoptosis	0.00000172	Increased	2.298	101
Cellular Compromise	stress response of cells	0.00235	Increased	2.63	8
Cellular Compromise, Cellular Function and Maintenance	endoplasmic reticulum stress response	0.000266	Increased	2.19	11
	endoplasmic reticulum stress response of cells	0.00129	Increased	2.219	6
Cell Cycle	M phase	0.000475	Decreased	-2.189	14
Cell Cycle, Cellular Movement	Cytokinesis	0.00148	Decreased	-2.189	11
Cell Morphology	orientation of cells	0.000019	Decreased	-2.121	13
Cellular Movement	migration of cells	0.00356	Decreased	-2.018	64
Gene Expression	transcription of DNA	0.000297	Decreased	-2.188	60

Supplementary Table 3. List of the top five networks generated using IPA.

Genes in network (Focus gene in bold)	**IPA score**	**No. of focus genes**	**Top functions**
Comparison between miNT and SCNT blastocysts derived from depleted cells			
AKT1S1, ATP1A1, ATP5B, ATP6AP2, CALB1, CALM1 (includes others), CAPZA2, FKBP1A, HIF3A, HMGN1, Insulin, **MLST8**, MTORC1, **NDUFA10**, NFkB (complex), **NOP58, NUCB2,** p70 S6k, **PDIA3**, PP2A, **PSMD12, RAP1GDS1, RHOC, RICTOR, RPL17, RPS6, RRAS2, RUVBL2,** SRC (family), **SUMO1, TAX1BP1, TFG, TPT1, UQCRB, WDR34**	40	29	Cancer, Organismal Injury and Abnormalities, Respiratory Disease
ACTB, BSG, DDX5, DSC2, DSG2, ERK, **HNRNPA1, HNRNPDL,** Hsp90, **HTATSF1, IGF2BP1, IPMK, JUP, KLF5, MET, MIF, MYL9, MYO1C, NPM1,** p85 (pik3r), **PLK1, PSMA3**, Rb, **RBBP8,** RNA polymerase II, Rnr, **RPS2, RPS3, RPS15A, SMAD5, SMG5, SNRNP200, TAGLN2, THOC1, UACA**	40	29	Cellular Development, Cellular Growth and Proliferation, Cardiac Arrythmia
26s Proteasome, Alp, **ATP6V1A, ATXN2L, BCL2L1, CBX3, CD47, CTSD, DBN1, DDB1, DDX6, DDX28**, Eif4g, **GALNT3, HEXA, HNRNPA2B1**, Hsp70, IL12 (family), **INTS3, MAPK8, MFN1, MOV10, NCOA1,** P-TEFb, **PMS1, POLR2A, PRDX3, PTOV1, RBBP6, RIMKLB, SUPT5H, SUPT6H, TFEB, TOB1, UPF3B**	40	29	Gene Expression, Cell Morphology, Cellular Function and Maintenance
ACTN1, ACTR2, ADAM9, Alpha tubulin, **CCDC22, CD2AP, CEP290, CKB, CLIC4, CLIP1, DGKZ,** Dynein, **DYNLT3**, ERK1/2, **FAM120A, FUT8**, Importin beta, **MADD**, MAP2K1/2, **MKS1**, NADPH oxidase, **NUMA1**, **PIK3CA, OLDIP3, PRDX2, RAB8B, RAD50, RAN, RAP1A, RPL23A, RPS6KB1, SMC3**, SYK/ZAP, **WASHC1, YES1**	38	28	Cellular Assembly and Organization, Cellular Function and Maintenance, Cell Morphology
Akt, **CEBPZ, CHORDC1,** Cofilin, **DNM2, ABP5, GNAI3, GNB4, HYOU1**, LDL, Mek, Mlc, **MYH9, NDUFV1, NRAS, PDCD10, PIP5K1C, PPP1R12A, PPP1R14A,** Ppp2c, **PPP2CA, PPP2R5D**, PRKAA, **RABGGTB**, Rock, **ROCK2, SDCBP, EC24A, SGO2, SMPD1, TFAM, TKT, UBA6, UBE3A, USP8**	36	27	Cell-To-Cell Signaling and Interaction, Cellular Compromise, Cell Signaling

miNT blastocysts derived from depleted cells cultured in the absence of TSA and SCNT blastocysts derived from depleted cells cultured in the presence of TSA			
ACTR2, ACTR3, ATN1, BAZ2A, BEND3, CAMSAP3, DMAP1, ELL2, H3F3A/H3F3B, Histone h3, **HTATSF1, IFITM3, JMJD1C, MGLL, MYSM1, NCAPD2, NMD3**, P-TEFb, **PHC1, PRRC2A, RAN, RAVER1,** RNA polymerase II, **RPL18, SF3A2, SF3B2, SH3GL1, SMC4, SNRPB2, SUPT5H, SUPT6H, SYNE2, THOC1, USP3, XIST**	39	32	DNA Replication, Recombination, and Repair, Gene Expression, Cell Cycle
ACO2, ALDOA, APH1A, APP, ARF4, ATP5B, ATP5D, ATP6V1A, BIN1, CDK5RAP2, CFL2, CKB, CLIC4, CLTB, CNTNAP1, CTSD, CXXC1, cytochrome C, **DYNLL2, EEF1G, GNMT, GPANK1, HIST1H2BD, MTHFD1L, MTHFR, NDUFA5,** Notch, **NPC1, SEC23A,** Secretase gamma, **SETD1A, SRFBP1, STX12, VPS29, VPS35**	39	32	Lipid Metabolism, Molecular Transport, Small Molecule Biochemistry
ADRM1, AP3D1, AP3S1, ATP6AP2, CALM1 (includes others), CAPZA2, CDC42EP1, Clathrin, **CLCN3, DYNC1H1, ECSIT, HIP1,** IL1, **LUC7L3, MAP3K7, MTDH,** NADPH oxidase, NFkB (complex), **PDCD11, PGD, PIAS4, PICALM, RAP1GDS1, RASSF5, RRAS2, SENP6, SMAD7,** Srebp, **SUMO1, TAB2, TAX1BP1, TRIM32, UBE2D3, WDR34, YES1**	35	30	Gene Expression, Cell Death and Survival, Decreased Levels of Albumin
ACADVL, ALAS1, AP1S2, CLK1, COTL1, DNMT3B, DPF2, ESRRA, FARP1, FASN, FOXO4, GALT, Hdac, **IFRD1, LHPP, MBNL1, MCRS1, MXD1**,N-cor, **NAMPT**, Nr1h, **PAF1, PDP1, PIAS1, POU5F1, PPRC1, PRDM14, PRPF6, PRRC2C, SBNO2, SEC62, SLC30A1,** Smad2/3, **SMARCA4**, Sos	35	30	Cellular Function and Maintenance, Gene Expression, Cellular Development
BAP1, CCNE2, CCNG1, CLN6, DCAF7, DHPS, DYRK1A, E2f, **ERO1A, FHL3, FURIN,** Gamma tubulin, hemoglobin, **HIF1A,** Hsp70, **HSPA4, LARP7, LMNB2, MCM3, MEF2D, NDRG1, ORC4, POLRMT**, Rb, **RBBP8, RECQL4, SKA2, SLC29A1, SMAD5, SMG5, SRSF2, TCEB1, TUBGCP5,** Ubiquitin, **XPNPEP2**	33	29	Developmental Disorder, Embryonic Development, Organismal Development

Comparison between miNT blastocysts derived from depleted cells cultured in the presence of TSA and SCNT blastocysts derived from depleted cells cultured in the presence of TSA			
Actin, Akt, **ANKRD1, CAPZB, DDX5, EIF2A, FHL3, GNAI3, GNB4,** Hsp90, **HTATSF1, KLHL2, LAMP1, MGLL, MYCBP, MYL9, MYO1C, NCL,** Notch, **NPM1, NRAS, OGG1, PIK3R2, PIP5K1C,** PP1 protein complex group, RNA polymerase II, Rnr, **RPS3, RPS6, RPS15A, S100A11, SDCBP, SRFBP1, SYCP3, TES**	41	28	Cancer, Hematological Disease, Organismal Injury and Abnormalities
ACTN4, B4GALT6, Cofilin, **DHFR, DMAP1, FABP5, HIP1, KLHL20,** LDL, **LUC7L3**, Mek, Mlc, **MPRIP, MTDH,** MTORC1, **NAMPT, NCOA4**, NFkB (complex), **NLRX1, PDCD11,** PP2A, **PPP1R12A, PRKAA1, PTPRA,** Rac, **RHOA, RND3, ROCK2, RRAS2, SLC7A5, SND1, SUMO1, SWAP70, TAX1BP1, YES1**	39	27	Cellular Growth and Proliferation, Cell-To-Cell Signaling and Interaction, Cellular Assembly and Organization
ACTN1, ARRB2, ATP1A1, CD9, CD2AP, CHORDC1, DNM2, Dynein, **DYNLT3, ELF1,** ERK1/2, Erm, **FKBP1A, GLIPR2, HLTF,** Integrin, **MOB4, MYH9, NBN,** p70 S6k, **PDCD10,** Ppp2c, **PTP4A2, PTPN12, RAD50, RAP1A,** Rock, RPA, **SLC39A10,** SRC (family), **TAPBP, THBD, TPR, TPT1, VCL**	37	26	Cell-To-Cell Signaling and Interaction, Cell-mediated Immune Response, Cellular Development
26s Proteasome, **ACADVL**, Alpha tubulin, AMPK, **ATP5B, ATP6V0D2, BCLAF1, BSG, CDK13, CHD1, CKB, CLIP1,** Cyclin E, **DNMT3B, DYNC1H1, ELL2,** ERK, **ERO1A, ESRRA, HIF1A, JAKMIP2**, mediator, **MGAT1**, Mitochondrial complex 1, **MTHFD1L, PDP1, PRRC2C, RTN4, SIRT1, STUB1,** TCR, **TOP1, UBR4, UCHL3,** Vegf	37	26	Cell-To-Cell Signaling and Interaction, Hematological System Development and Function, Immune Cell Trafficking
ACTB, AP1S2, BRD7, CEP170, Cg, **COTL1**, Creb, **DNAJB9**, estrogen receptor, **FASN**, FSH, Gsk3, Hdac, Histone h3, Histone h4, **JMJD1C, KDM5C,** Lh, **MAF1, MXD1, MYSM1**, Nr1h, **PIAS1**, Rb, **RBBP8, RNASEH2A**, Smad2/3, **SMARCA4, SMC4**, Sos, **SYNE2, TAGLN2, TM4SF1, TSPAN13, XIST**	29	22	Cellular Development, Cellular Growth and Proliferation, Embryonic Development

Bold type indicates that the genes are present in the RNA-seq data. Non-bolded type indicates that the genes are directly associated with the bold genes, which were obtained from the Ingenuity Knowledge Base.

Supplementary Table 4. List of biological processes from common DEGs amongst the three comparisons.

Biological process (Gene Ontology)	**No. of gene**	**%***	**Gene**
Biological adhesion (GO:0022610)	3	1.9	*RAP1A, NRAS, ROCK2*
Biological regulation (GO:0065007)	8	5.1	*BCL2L1, GNAI3, LIN7C, FAM60A, ATP1A1, YES1, CSNK1G3, DZIP3*
Cellular component organization or biogenesis (GO:0071840)	27	17.1	*UQCRB, RPL23A, ACTB, RAN, ATAD1, TOP1, CLIP1, RPS6, RPL23A, MYH9, RPL23A, ROCK2, TFIP11, ACTN4, DNM2, TMEM33, FAM96A, SMC4, NOP58, ACTN1, CSNK1G3, USO1, RICTOR, FLNB, DYNC1H1, DYNLT3, RPL7*
Cellular process (GO:0009987)	74	46.8	*RRAS2, SEPT7, AMD1, ARF4, PSMD12, SMAD5, BCL2L1, RAP1A, GNAI3, HTATSF1, CDC27, RNASEH2A, UQCRB, CHORDC1, RAB6A, LIN7C, GNB4, RPL23A, FAM60A, SYNE2, ACTB, RPS3, RAN, CEP135, NRAS, ATAD1, TOP1, ATP1A1, CLIP1, RASA2, RPS6, KIF20B, BSG, S100A16, DDX5, ZCCHC11, PDP1, RPL23A, PAPOLA, KLHL2, VPS35, MYH9, RPL23A, ROCK2, MOSPD3, MYO1C, TFIP11, STEAP3, YES1, HMGA1, ACTN4, MAGI3, DNM2, TMEM33, FAM96A, FKBP1A, PPIG, SMC4, POP7, RBBP8, NOP58, SUMO1, ZMYM1, ACTN1, HIAT1, CSNK1G3, USO1, RICTOR, DZIP3, FLNB, DYNC1H1, DYNLT3, PIP5K1C, RPL7*
Developmental process (GO:0032502)	10	6.3	*BCL2L1, SYNE2, UBE2D3, CLIP1, PTGR2, MYH9, ROCK2, MYO1C, YES1, MYL9*
Immune system process (GO:0002376)	2	1.3	*YES1, S100A16*
Localization (GO:0051179)	28	17.7	*RRAS2, ARF4, RAP1A, AP3S1, RAB6A, LIN7C, FAM60A, ACTB, RAN, NRAS, CLIP1, VPS35, MYH9, TMED5, MOSPD3, MYO1C, STEAP3, YES1, TMED2, DNM2, TMEM33, ERO1L, CSNK1G3, REEP3, USO1, DYNC1H1, DYNLT3, SDCBP*
Locomotion (GO:0040011)	2	1.3	*FAM60A, YES1*
Metabolic process (GO:0008152)	66	41.8	*AMD1, PSMD12, SMAD5, THAP5, GNAI3, ATP5B, HTATSF1, PQLC3, RNASEH2A, UQCRB, CD2AP, RPL23A, UBE2D3, HSP90B1, RPS3, RAN, ATAD1, TOP1, ATP1A1, CLIP1, RASA2, PDPR, RPS6, KIF20B, S100A16, DDX5, SSB, PTGR2, PDP1, RPL23A, GDPD5, PAPOLA, HRSP12, KLHL2, THOC2, RPL23A, TFIP11,*

			EPC2, PPP1R12A, UPF3B, YES1, HMGA1, PRRG4, FAM96A, FKBP1A, PPIG, SMC4, POP7, LARP4, RBBP8, NOP58, SUMO1, ERO1L, ZMYM1, SND1, JMJD1C, NPM1, MXD1, CSNK1G3, REEP3, RICTOR, DZIP3, RBBP6, DYNLT3, PIP5K1C, RPL7
Multicellular organismal process (GO:0032501)	9	5.7	*RAP1A, LIN7C, GNB4, NRAS, MYH9, MYO1C, MAGI3, MYL9, TAGLN2*
Reproduction (GO:0000003)	1	0.6	*DYNC1H1*
Response to stimulus (GO:0050896)	11	7.0	*BCL2L1, GNAI3, RNASEH2A, HSP90B1, RPS3, RASA2, YES1, HMGA1, CSNK1G3, RICTOR, DZIP3*

*Percent of gene hit against total number of genes (158 DEGs).

Supplementary Table 5. List of biological processes from unique DEGs for the comparison between miNT blastocysts derived from depleted cells cultured in the absence of TSA and SCNT blastocysts derived from depleted cells cultured in the presence of TSA.

Biological process (Gene Ontology)	**No. of gene**	**%***	**Gene**
biological adhesion (GO:0022610)	11	2.1	*TNS1, CNTNAP1, ITGA5, CBLL1, COL17A1, COLGALT1, SCARB1, PLOD3, PLXNB2, NLGN2, RAP2C*
biological regulation (GO:0065007)	42	8.0	*PAK1, NDRG1, MAP3K7, TIMP1, TIMP2, AZIN1, AKT3, GNA11, CD63, NUCB2, ATAD2B, PLSCR1, SPNS1, RAP1GDS1, KRCC1, SLK, BAHD1, CBLL1, LATS1, SNAP23, PPRC1, CDC37,ADCY9 ,ESPL1 ,BCKDK ATXN2L, ACAD11, SLC30A1, EIF4A2, RAB8B, BOK, TANK, MAP2K2, PLXNB2, STX4, NLGN2, BAIAP2, PRKCZ, FKBP9, RPS6KA1, MASTL, GNAS*
cellular component organization or biogenesis (GO:0071840)	66	12.6	*CAPZA2, PAK1, SMC3, BRD3, HAT1, CLTB, DKC1, CFL2, DTNB, FLNC, POMT2, H3F3A, SNX10, BRWD1, KRT80, SF3B1, METTL17, PES1, LMNB2, H3F3A, STX12, XAB2, PLSCR1, CDC42EP1, TBC1D17, IPO4, BAHD1, EDC3, MTFR2, TUBGCP5, PRPF8, SASS6, HSPA4, COL17A1, SNAP23, PRPF6, NUP54, DDX6, ESPL1, SUPT6H, ATXN2L, GSN, SNX4, RAB8B, GNL1, WDR34, WASF1, TMOD3, CCT3, PLXNB2, STX4, ASF1A, NCAPD2, CBX3, NLGN2, BAIAP2, DNAH2, CCDC28B, KRT8, RPSA, TAF1B, ACTR3, KIF18B, CDK5RAP2, WASF2, DBN1*
cellular process (GO:0009987)	239	45.6	*CAPZA2, PAK1, ARHGDIA, SMC3, NDRG1, NEURL4, MAP3K7, TBK1, AFF1, ZFYVE16, BRD3, GSK3A, TIMP1, PPWD1, HAT1, CLTB, CALM, DKC1, NDUFB9, TIMP2, CFL2, SHROOM3, CTSA, DTNB, TNS1, FLNC, CNTNAP1, RASA1, POMT2, RPL29, OGT, H3F3A, SNX29, SNX10, NDNL2, RECQL4, RHOB, PCDH1, PIK3CA, AZIN1, AKT3, PDXK, SYMPK, BRWD1, GNA11, PIGN, CD63, EIF3L, SIRT7, CDKN3, BAZ2B, KRT80, PPP2CB, SF3B1, CDC42BPA, ABR, KAT5, EHD1, PES1, FOXO4, LMNB2, CTSD, H3F3A, SERINC2, RHOV, STX12, XAB2, ATAD2B, SENP6, VPS54, LOC531152, MOV10, PLSCR1, MTA2, UBE2J1, SPNS1, RAP1GDS1,*

			CDC42EP1, LIG1, PFAS, SMAD7, RAVER1, KRCC1, SF3B2, SLK, TBC1D17, MLXIP, TRRAP, IPO4, CDC25A, ADA, BAHD1, EDC3, DDB1, CCNG1, RAB3IP, LOC515358, FTSJ1, CBLL1, SNRPB2, ATN1, MTFR2, TUBGCP5, PRPF8, MLXIPL, EIF3D, TUFM, CLTC, RPL8, SLC5A11, CTAGE5, PLEKHG3, CCNE2, DPF2, PPIL4, NPC1, RASSF5, LATS1, SASS6, LIN54, PLK1, CALM, COL17A1, RNPC3, SPTAN1, MTHFR, NR2C2AP, DAB2IP, PGM1, DNALI1, SNAP23, NUDC, PRPF6, NUP54, PPIA, B3GNT5, PPRC1, LGALS9, CSTF3, THOC1, CDC37, PIGK, RPL18, B3GNT3, ADCY9, MCM3, CLDN10, DDX6, APP, ESPL1, RHOV, SUPT6H, BCKDK, ATXN2L, ACAD11, RAB1B, EEF2, SLC30A1, TSEN54, ERCC2, PKIA, DSG2, GSN, EIF4A2, COLGALT1, SNX4, GLS, RAB8B, CNOT7, SLC25A6, EEF1G, GNL1, ABCA3, SUPT5H, EIF3B, TCEB1, BOK, TANK, BAZ2A, WDR34, FOXP4, SPIC, MYBL2, SOD1, EPN2, SCARB1, IGF2BP1, NCOA1, IQGAP3, YWHAQ, RCOR2, TMOD3, MAP2K2, PLXNB2, STX4, DSC2, TTK, SEC23A, ASF1A, TMEM189, NCAPD2, CBX3, BAIAP2, PRKCZ, DNAH2, ITPR1, KIF21A, CCDC28B, CLINT1, CCNF, KRT8, FKBP9, POLR2H, CDS2, RPSA, ATP5D, SLC25A1, SLC7A8, TAF1B, ACTR3, GEN1, CLIC4, PRKAR1A, KIF18B, CDK5RAP2, RPS6KA1, DTD1, ADRM1, RAPGEF1, RPS9, MIER1, DDX41, PARP1, MASTL, RAP2C, SLC7A4, DBN1, GNAS, FGGY
developmental process (GO:0032502)	34	6.5	*PAK1, PCNXL3, NEURL4, ADAM9, ILF3, GSK3A, TNS1, FARP1, CNTNAP1, PCDH1, CDC42BPA, FOXO4, ZC3H10, MEF2D, VAT1,KRCC1 ,SLK ,DPF2 ,RASSF5, LATS1, IFRD1, B3GNT5, THOC1, B3GNT3, BOK, FOXP4, SPIC, IGF2BP1, TMOD3, MAP2K2, PLXNB2, NLGN2, CDK5RAP2, MIER1*
growth (GO:0040007)	1	0.2	*LATS1*
immune system process (GO:0002376)	13	2.5	*PRKAB1, TBK1, ILF3, ABCC1, TNS1, CNTNAP1, PTGS2, PLEKHG3, HSPA4, COL17A1, GPX2, GPX1, ITPR1*
localization (GO:0051179)	69	13.2	*MAL2, PAK1, ZFYVE16, CLCN3, ILF3, XPO1, AP3D1, CLTB, NDUFB9 ,SLC35A1, SHROOM3, ABCC1, TMED1, TTYH2, CNTNAP1, TRAM2, SNX29, SNX10, RHOB, EHD1, CHMP2B, SERINC2, RHOV, STX12, VPS54, LOC531152, PLSCR1, TBC1D17, IPO4, REEP5, AP1B1, CLTC, SLC5A11, CPNE2, NPC1, POLDIP3, NUP54 ,THOC1, PIGK, APP, RHOV, RAB1B, AP1B1, SLC29A1, SLC35A3, SNX4, DDHD1, RAB8B, ABCA3, WDR34, EPN2, IGF2BP1, MCFD2, SCAMP4, STX4, SEC23A, NLGN2, DNAH2, ITPR1, RPSA, PICALM, SLC7A8, ACTR3, CLIC4,*

			CDK5RAP2, SEC14L1, RAP2C, SLC7A4, SLC46A1
locomotion (GO:0040011)	1	0.2	*PAK1*
metabolic process (GO:0008152)	217	41.4	*CREG1, PAK1, SMC3, PRKAB1, MAP3K7, AFF1, PRODH, DHPS, ANXA5, BRD3, GSK3A, XPO1, TIMP1, PPWD1, HAT1, DKC1, NDUFB9, TIMP2, ATMIN, PRRC2A, SLC35A1, PFKFB4, CTSA, SRSF2, TNS1, CNTNAP1, RASA1, TRAM2, POMT2, RPL29, MVK, OGT, H3F3A, PHF3, RECQL4, PRPSAP1, ATP6V1A, MDFIC, PIK3CA, AZIN1, AKT3, PDXK, BRWD1, RBM10, GNA11, PGD, PIGN, EIF3L, SIRT7, CDKN3, BAZ2B, PPP2CB, SF3B1, ABR, ZNF335, KAT5, PIAS4, HSPB6, PES1, FOXO4, CTSD, GALT, H3F3A, ACO2, XAB2, ATAD2B, ZNF592, ANXA3, MOV10, MTA2, UBE2J1, RAP1GDS1, CDC42EP1, LIG1, PFAS, BTF3, SMAD7, VAT1, CBR4, RAVER1, SF3B2, SLK, MLXIP, TRRAP, SBNO2, CDC25A, RPLP1, ADA, BAHD1, EDC3, DDB1, ALAS1, ARL14EP, REEP5, GALNT1, FTSJ1, CBLL1, SNRPB2, GNE, ENPP5, MTFR2, PRPF8, MLXIPL, EIF3D, TUFM, RPL8, DPF2, TGM2, CAPN5, PPIL4, NPC1, LATS1SASS6, RPAP3, PTOV1, RNPC3, POLDIP3, PFKL, NR2C2AP, DAB2IP, PGM1, PRPF6, PCMTD1, PPIA, B3GNT5, PPRC1, RAD23B, CSTF3, THOC1, CDC37, PIGK, GPX2, RPL18, B3GNT3, ADCY9, MCM3, DDX6, TKT, SUPT6H, BCKDK, NPL, ACAD11, EEF2, GPX1, TSEN54, ERCC2, PKIA, TLE3, APH1A, SLC29A1, EIF4A2, POLRMT, SLC35A3, COLGALT1, KLK6, GLS, CNOT7, SLC25A6, EEF1G, GNL1, GALNT3, ABCA3, SUPT5H, EIF3B, TCEB1, TANK, CXXC1, BAZ2A, WDR34, FOXP4, SPIC, MYBL2, TAB2, GF2BP1, NCOA1, IDH3B, RCOR2, ESRP2, MAGT1, CCT3, MAP2K2, AGPS, PLXNB2, LHPP, NDUFA5, SMYD5, TTK, ASF1A, TMEM189, NCAPD2, CBX3, LSM14A, PRKCZ, KIF21A, FKBP9, POLR2H, CDS2, GAPDH, RPSA, ATP5D, SLC25A1, LARGE, TAF1B, GEN1, CLIC4, KIF18B, RPS6KA1, DTD1, ZNF408, SEC14L1, RPS9, MIER1, DDX41, PARP1, MASTL, GNAS, FGGY*
multicellular organismal process (GO:0032501)	22	4.2	*ADAM9, ILF3, CNTNAP1, PCDH1, DNAJC3, EHD1, LOC531152, RAB3IP, CLTC, PLEKHG3, LATS1, SNAP23, RAB8B, EPN2, IGF2BP1, TMOD3, PLXNB2, STX4, ITPR1, CLINT1, RAP2C, GNAS*
reproduction (GO:0000003)	13	2.5	*NEURL4, ADAM9, ILF3, NDNL2, CCNG1, TUBGCP5, CCNE2, LIN54, B3GNT5, B3GNT3, ESPL1, NCAPD2, CCNF*
response to stimulus (GO:0050896)	46	8.8	*PAK1, NDRG1, PRKAB1, MAP3K7, TIMP1, TIMP2, ABCC1, CNTNAP1, RASA1, RECQL4, AKT3, GNA11, CD63, PPP2CB, HSPB6, SPNS1, RAP1GDS1,*

			CDC42EP1, LIG1, SMAD7, KRCC1, SLK, TRRAP, DDB1, MLXIPL, PLEKHG3, LATS1, RPAP3, DAB2IP, GPX2, ADCY9, SLC30A1, GPX1, BOK, TANK, SOD1, NCOA1, MCFD2, MAP2K2, BAIAP2, PRKCZ, ITPR1, RPS6KA1, PARP1, MASTL, GNAS

*Percent of gene hit against total number of genes (524 DEGs).

Supplementary Table 6. Effects of mitochondrial supplementation on the biological function of miNT blastocysts when compared with SCNT blastocysts derived from depleted cells cultured in the presence of TSA.

Categories	Functions annotation	p-Value	Predicted State	Activation z-score	No. of genes
Carbohydrate metabolism	glycolysis of cells	0.000747	Increased	2.412	10
Cell cycle, DNA Replication, recombination, and repair	DNA recombination	0.0000199	Increased	2.151	16
	homologous recombination	0.00000851	Increased	2.177	14
	homologous recombination of cells	0.0000011	Increased	2.514	13
Cellular assembly and organization, cellular function and maintenance	microtubule dynamics	0.00317	Increased	2.345	58
	organization of cytoskeleton	0.000165	Increased	2.639	73
	organization of cytoplasm	0.000775	Increased	2.639	76
Cellular assembly and organization	formation of cytoplasmic aggregates	0.000268	Decreased	-2.176	6
Embryonic development, organismal survival	death of embryo	0.0000934	Decreased	-2.028	14
Gene expression	expression of mRNA	0.00241	Decreased	-2.414	14
Gene expression, protein synthesis	translation of mRNA	0.00154	Decreased	-2.2	13
Organismal survival	organismal death	3.79E-14	Decreased	-3.644	156
	morbidity or mortality	5.54E-14	Decreased	-3.566	157
Protein synthesis	modification of peptide	0.0000429	Decreased	-2.236	12
	metabolism of peptide	0.00137	Decreased	-2.236	14

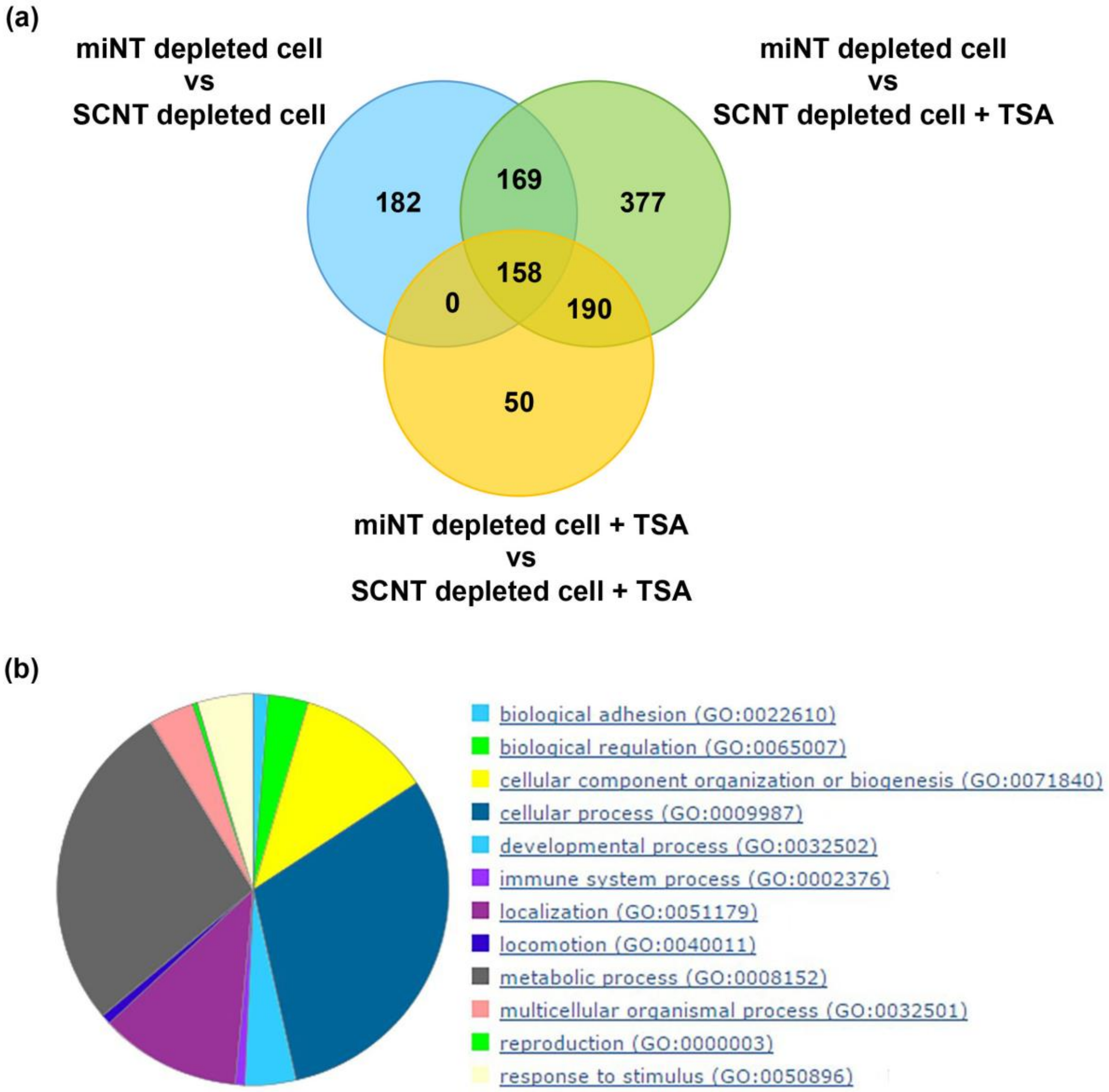
Supplementary Table 7. List of biological processes from unique DEGs from the comparison between miNT blastocysts derived from depleted cells cultured in the presence of TSA and SCNT blastocysts derived from depleted cells cultured in the presence of TSA.

Biological process (Gene Ontology)	**No. of gene**	**%***	**Gene**
biological regulation (GO:0065007)	4	8.2	*CD9, SLC34A2, SLC39A10, LSCR4*
cellular component organization or biogenesis (GO:0071840)	5	10.2	*NES, VBP1, RTN4, SIRT1, PLSCR4*
cellular process (GO:0009987)	16	32.7	*CD9, OGG1, PPP3CC, SLC25A11, NES, RABGGTA, LOC534630, UCHL3, VBP1, GCGR, ANKRD1, SLC34A2, RNF145, SLC39A10, SIRT1, PLSCR4*
developmental process (GO:0032502)	6	12.2	*PPP3CC, PBX3, DLX4, GCGR, ANKRD1, RTN4*
immune system process (GO:0002376)	3	6.1	*PPP3CC, GCGR, GLIPR2*
localization (GO:0051179)	6	12.2	*LOC534630, GCGR, SLC34A2, BCAP29, PLSCR4, NUP214*
metabolic process (GO:0008152)	17	34.7	*OGG1, PPP3CC, SLC25A11, RABGGTA, PBX3, DLX4, ACER3, LOC534630, SH3D21, UCHL3, PTPRA, CHSY1, DCPS, ANKRD1, PPA1, RNF145*
multicellular organismal process (GO:0032501)	4	8.2	*GCGR, ANKRD1, RTN4, CNN3*
reproduction (GO:0000003)	2	4.1	*GCGR, GLIPR2*
response to stimulus (GO:0050896)	5	10.2	*CD9, OGG1, PPP3CC, ACER3, GCGR*

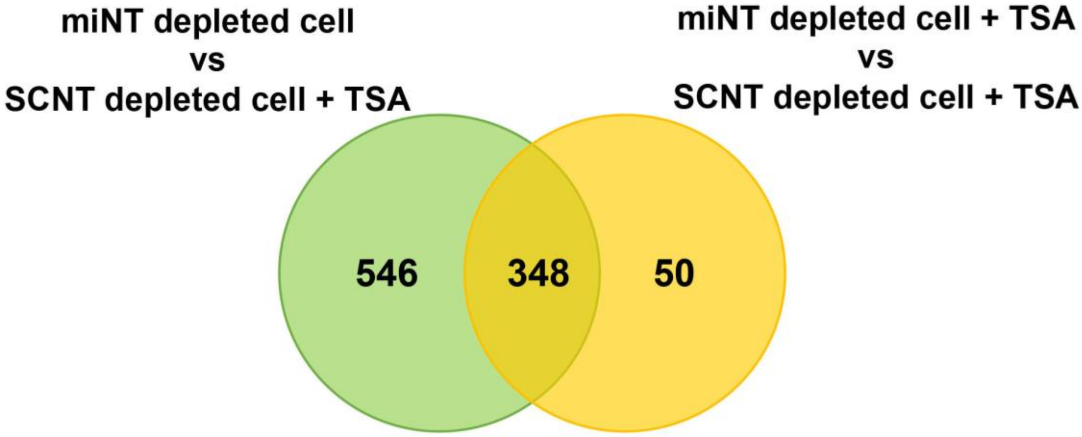
*Percent of gene hit against total number of genes (49 DEGs).

Supplementary Table 8. List of the significant differentially expressed genes from the comparison between miNT blastocysts derived from depleted and nondepleted cells. Fold changes are relative to miNT blastocysts derived from nondepleted cells.

ID	**Fold change**	**Regulation**	**FDR**	**Entrez Gene Name**	**Entrez gene ID**	**Location**	**Type(s)**
TMEM219	63.88560243	Up	0.0265	transmembrane protein 219	506622	Plasma Membrane	other
APLP1	60.1000964	Up	0.0265	amyloid beta precursor like protein 1	513154	Extracellular Space	other



Supplementary Figure 1. Common DEGs amongst the three comparisons. (a) Venn diagram showing common DEGs amongst the comparisons between miNT and SCNT blastocysts derived from depleted cells cultured in the absence of TSA (blue); miNT blastocysts derived from depleted cells cultured in the absence of TSA and SCNT blastocysts derived from depleted cells cultured in the presence of TSA (green); and miNT and SCNT blastocysts derived from depleted cells cultured in the presence of TSA (Yellow) are shown. (b) PANTHER biological process classification.



Supplementary Figure 2. Common DEGs between two comparisons. Venn diagram shows common and unique DEGs between comparisons of miNT blastocysts derived from depleted cells in the absence of TSA and SCNT blastocysts derived from depleted cells cultured in the presence of TSA (green); and miNT and SCNT blastocysts derived from depleted cells cultured in the presence of TSA (Yellow).