

Molecular Mechanisms of Increased Heart Rate in Shenxianshengmai-treated Bradycardia Rabbits

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Abstract

Background: The molecular mechanisms of Shenxianshengmai (SXSM), a traditional Chinese medicine, on bradycardia have been incompletely understood. The study tried to investigate the gene expression profile and proteomics of bradycardia rabbits' hearts after SXSM treatment.

Methods: Twenty-four adult rabbits were randomly assigned in four groups: sham, model, model plus SXSM treatment, and sham plus SXSM treatment groups. Heart rate was recorded in all rabbits. Then, total RNA of atria and proteins of ventricle were isolated and quantified, respectively. Gene expression profiling was conducted by gene expression chip, and quantitative real-time reverse transcription-polymerase chain reaction (RT-PCR) was performed to confirm the results of gene expression chip. We used isobaric tags for relative and absolute quantitation and Western blotting to identify altered proteins after SXSM treatment.

Results: There was a constant decrease in the mean heart rate (32%, from 238 ± 6 beats/min to 149 ± 12 beats/min) after six weeks in model compared with that in sham group. This effect was partially reversed by 4-week SXSM treatment. Complementary DNA microarray demonstrated that the increased acetylcholinesterase and reduced nicotinic receptor were take responsibility for the increased heart rate. In addition, proteins involved in calcium handling and signaling were affected by SXSM treatment. Real-time RT-PCR verified the results from gene chip. Results from proteomics demonstrated that SXSM enhanced oxidative phosphorylation and tricarboxylic acid (TCA) cycle in ventricular myocardium to improve ATP generation.

Conclusions: Long-term SXSM stimulates sympathetic transmission by increasing the expression of acetylcholinesterase and reduces the expression of nicotinic receptor to increase heart rate. SXSM also restored the calcium handling genes and altered genes involved in signaling. In addition, SXSM improves the ATP supply of ventricular myocardium by increasing proteins involved in TCA cycle and oxidation-respiratory chain.

Key words: Gene Expression; Heart Rate; Proteomics; Shenxianshengmai

INTRODUCTION

Bradycardia is a condition in which pulse rate is below 60 beats/min. Coronary artery disease patients and elderly people are at a great risk of developing the abnormally slow heart rate.^[1] Currently available drugs (e.g., atropine, dopamine, isoproterenol, and epinephrine) treating bradycardia are temporizing measures only in emergency settings. If the patient does not respond to drugs, temporary or permanent cardiac pacemaker is probably indicated.^[2] However, the cost of pacing put a huge financial burden on the family. Consequently, an effective drug aiming at increasing heart rate for a long-term is in urgent demand.

The Traditional Chinese Medicines have been used to treat arrhythmia for hundreds of years and Shenxianshengmai (SXSM) is one of such medicines. It is a product consisting of eight ingredients including *Radix Ginseng Rubra*, *Herba*

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Epimedium Brevicornus, *Fructus Psoraleae*, *Fructus Lycii*, *Herba Ephedrae Sinicae*, *Asarum Heterotropoides*, *Radix Salviae Miltiorrhizae*, and *Hirudo*. Clinical researches demonstrated that SXSM is effective in treating bradycardia.^[3-7] However, it has been a mystery how SXSM plays the positive role in treatment. Therefore, we use a bradycardiac animal model to explore the molecular mechanisms of SXSM treatment. Our work will provide new insights into the mechanisms of SXSM.

METHODS

Bradycardia model

Twenty-four adult rabbits (*Oryctolagus cuniculus*) with mean body weight of 2.5 ± 0.5 kg were used for the study. The experimental protocol was performed in accordance with the Guide for the Care and Use of Laboratory Animals (NIH Publication No. 85-23, revised 1985) and the ARRIVE.^[8] The Care of Experimental Animals Committee of the Chinese Academy of Medical Sciences and Peking Union Medical College approved the procedures for the care and treatment of animals. The animals were randomly divided into four groups ($n = 6$ in each group): sham, model, sham plus SXSM (S+XSSM), and model plus SXSM (M+XSSM) groups. Sterilized cotton bud with formaldehyde (37%, SCRC, China) was fixed on the wall of the right atrium, near the entrance of the superior vena cava until heart beat decreased 25–35%.^[9] The procedures were the same as the previous study.^[10] Then, purified water was administered orally to model group while SXSM ($275 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$) was administered to blank plus SXSM and M+XSSM groups. Lead II was used to monitor the electrocardiogram, once every week for 4 weeks. At last, animals were sacrificed 6 weeks later. The procedures in sham and S+XSSM groups were similar to model and M+XSSM groups except that formaldehyde was replaced by purified water. RR, P, PR, QRS, QT, and QTc were calculated before operation (baseline) and 6 weeks' later, respectively.

RNA and protein preparation

Hearts of the animals were isolated and perfused with purified water. Atria and ventricle of the heart were immediately frozen in liquid nitrogen and then stored at -80°C until use for RNA extraction. MirVana™ mRNA isolation kit (Ambion-1561, USA) was used in accordance with the manufacturer's instructions to isolate total RNA. Then, NanoDrop ND-2000 (Thermo Scientific, USA) and Agilent Bioanalyzer 2100 (Agilent Technologies, USA) were used to quantify RNA and assess the RNA integrity, respectively. To minimize variations attributable to individual rabbit and maximize differences attributable to their genotype, each experiment was performed with RNA pooled from 3 atria. Ventricular tissues were homogenized in 5 volumes (v/w) of isolation buffer (300 mmol/L sucrose, 10 mmol/L HEPES/Na, 500 $\mu\text{mol/L}$ ethylenediaminetetraacetic acid (EDTA)•2Na, pH 7.4, 2 mmol/L phenylmethyl sulfonyl fluoride (PMSF) and 1:1000 diluted Protease Inhibitor Cocktail (Sigma P8340, USA) using a Dounce Glass/Teflon Homogenizer

according to the method of Frezza *et al.*^[11] Centrifugation was carried out twice, $800 \times g$, 4°C for 10 min.

Gene expression profiling

Total RNA was transcribed to double-strand complementary DNA (cDNA), then synthesized into cRNAs and labeled with Cy3. Labeled cRNAs were hybridized onto Agilent Rabbit Gene Expression Chip (4*44K, Design ID: 020908, containing 43,803 probes) according to manufacturer's instructions and scanned by Agilent Scanner G2505C (Agilent Technologies). Feature Extraction software (version 10.7.1.1, Agilent Technologies) was used to analyze array images to get raw data. Data normalization was performed using GeneSpring. Differentially expressed genes were selected based on fold-change >2.0 and $P < 0.05$ according to two-way analysis of variance (ANOVA). Gene ontology (GO) database and KEGG were applied to determine functions of these differentially expressed messenger RNAs (mRNAs).^[12] Then, differentially expressed genes were researched by Funnet and Uniprot database (<http://www.uniprot.org>).

Quantitative polymerase chain reaction

SYBR Green quantitative real-time reverse transcription-polymerase chain reaction (RT-PCR) was performed on the genes ATP2A1, ERP27, FKBP1B, MBIP, and 18S rRNA (as an internal control) to confirm the results of gene expression chip. Genes were selected from interesting functional groups revealed by GO analysis [Table 1].^[13-32] Primers were designed with LightCycler Probe Design software 2.0 (Roche Applied Bioscience, Swiss). The cDNA was synthesized at 37°C for 15 min in a 10 μl reaction containing 0.5 μg total RNA, 2 μl PrimerScript Buffer, 0.5 μl oligo dT, 0.5 μl random 6mers and 0.5 μl PrimerScript RT Enzyme Mix I (TaKaRa, Japan). Real-time RT-PCR reactions included 1 μl of cDNA, 5 μl $2 \times$ LightCycler® 480 SYBR Green I master mix (Roche), 0.2 μl forward primer, 0.2 μl reverse primer, and 3.6 μl water of nuclease-free. All PCR reactions were carried out in triplicate with the following conditions: 95°C for 10 min, followed by 40 cycles of 10 s at 95°C , 30 s at 60°C in the LightCycler® 480 II Real-time PCR Instrument (Roche). For each selected gene, melting curve analysis was performed to validate the specific generation of the expected PCR product. The expression of each gene was normalized as ΔC_t (C_t of target gene – C_t of internal control gene) using 18S rRNA as the control. Relative quantification using the $\Delta\Delta C_t$ method was applied to compare the amounts of mRNA in sham versus model groups and model versus SXSM groups.^[33]

Protein preparation and isobaric tags for relative and absolute quantitation labeling

Protein preparation from rabbits was performed following the published method^[34] with some modifications. Briefly, ventricles from three rabbits were pooled and homogenized in 5 volumes (v/w) of isolation buffer (0.3 mol/L sucrose, 10 mmol/L HEPES-Na, pH 7.0, 0.5 mmol/L EDTA, 2 mmol/L PMSF, and 1:1000 diluted Protease Inhibitor Cocktail [Sigma P8340]) using a Dounce Glass/Teflon Homogenizer. Centrifugations were carried out twice to discard nuclear and

Table 1: Candidate genes associated with increased heart rate

Function	Gene symbol	Protein name	Average Log ₂ FC (model)	P (model)	Average Log ₂ FC (drug)	P (drug)
Increase heart rate ^[13-17]	ACE-1	Acetylcholinesterase			1.21	0.026
N-receptor ^[18]	CHRNA2	Cholinergic receptor, nicotinic, alpha 2			-1.05	0.0001
Re-uptake Ca ²⁺ to ER ^[19,20]	ATP2A1	ATPase, Ca ²⁺ transporting, cardiac muscle	-1.55	0.0027	1.31	0.003
Protein disulfide isomerase (ER) ^[21]	ERP27	Endoplasmic reticulum resident protein 27	-2.07	0.037	2.63	0.005
Calcium homeostasis ^[22-24]	FKBP1B	FK506-binding protein, 12,600	-1.19	0.024	1.13	0.043
Inhibit MAP3K12, inhibit JNK/SAPK pathway ^[25]	MBIP	MAP3K12 binding inhibitory protein 1	1.11	0.009	-1.11	0.008
Isomerase, participate in ER redox homeostasis ^[26,27]	PPIC	Peptidylprolyl isomerase C (cyclophilin C)	-1.06	0.015	1.26	0.004
Intracellular signaling pathways ^[28]	PRKCZ	Protein kinase C, zeta	1.71	0.022	-1.75	0.019
Activate AC ^[29]	VIPRI	Vasoactive intestinal polypeptide receptor 1	2.75	0.027	-2.96	0.016
Signaling ^[30]	PRLR	Prolactin receptor	-1.57	0.004	1.23	0.023
Protein phosphorylation ^[31]	NIM1K	Serine/threonine-protein kinase NIM1	5.31	0.030	-3.61	0.001
Undefined	LOC100355813	Olfactory receptor GPCR1TM7	-1.09	0.012	-1.03	0.005
Metalloendopeptidase activity ^[32]	MMP1	Matrix metalloproteinase 1 (interstitial collagenase)	-1.38	0.015	-1.11	0.003

FC: Fold change; *P*: *P* value calculated from two double-factor variance analysis. ER: Endoplasmic reticulum; SXSM: Shenxianshengmai.

cell debris, 800 ×g, 4°C for 10 min. The supernatant was then collected and stored at -80°C.

To minimize variations attributable to individual rabbit and maximize differences attributable to their genotype, each experiment was performed with RNA pooled from three ventricles. Equal amounts of protein (75 µg) from each pooled sample were digested with trypsin (0.5 µg/µl) at 37°C for 16h and labeled with unique isobaric tags for relative and absolute quantitation (iTRAQ) reagent (114 for model group, 115 for SXSM group). Labeled samples were pooled and dried in a vacuum centrifuge.

Isobaric tags for relative and absolute quantitation proteomic analysis

The labeled dried peptides were dissolved in mobile phases A (2% acetonitrile [ACN], pH 10.0). Then, samples were loaded on the reversed phase column (Agela, 5 µm, 150 Å, 4.6 mm × 250 mm,) and separated on an L-3000 HPLC system (Rigol, China) at a flow rate of 1 ml/min. Mobile phase A consisted of 2% ACN and mobile phase B consisted of 98% ACN. Both of them were adjusted pH to 10.0 using NH₃·H₂O. The gradient used was described as following: 5–8% B, 2 min; 8–18% B, 11 min; 18–32% B, 9 min; 32–95% B, 1 min; 95% B, 1 min; 95–5% B, 2 min. The temperature of Column Oven was set as 60°C. Fractions were collected every minute and then dried in a vacuum centrifuge. Forty fractions were collected and desalted. Then, fractions were combined into twelve fractions and vacuum-dried until analyzed by LC/MS/MS.

After dissolved in 0.2% fatty acid and 5% methanol, the dried tryptic peptides loaded and trapped on a precolumn

(C₁₈, 100 µm × 20 mm, 5 µm particle size), then separated on an analytical column (C₁₈, 75 µm × 150 mm, 3 µm particle size). Peptides were eluted from the C₁₈ analytical column with 40-min gradient at a flow rate of 350 nL/min on Eksigent Ultra HPLC (AB Sciex). The MS conditions for TripleTOF 5600 were set as the followings: the spray voltage was set of 2.5 kv and the temperature of heater was 150°C. The MS scan range was set at 350 to 1250 m/z and the MS/MS scan range was 100–1500 m/z. Data-dependent acquisition was performed and top 50 precursor ions were selected to fragment using collision induced dissociation (CID). The collision-induced dissociation energy was automatically adjusted by the rolling CID function.

Database search and bioinformatics

The resulting MS/MS data were then compared against data in the NCBI database (Rabbit.protein-20150201) using ProteinPilot™ Software Beta (version 4.5, AB, USA). For protein identification and quantification, peptide mass tolerance and fragment tolerance were each set at 0.3 Da. Only one missed tryptic cleavage was allowed. The false positive rates were controlled below 1%. The following criteria were used to select differentially expressed proteins: (1) proteins including at least one unique high-scoring peptide; (2) *P* < 0.05; and (3) fold-changes needed to be >2 or <0.5. The UniProt knowledge base (Swiss-Prot/TrEMBL, <http://www.uniprot.org/>) and GO database were applied to further classify these differentially expressed proteins.

Western blotting

Samples were prepared in SDS sample buffer, separated on

10% SDS gel, and transferred to 0.45 μm polyvinylidene fluoride membranes. The membranes were incubated with primary antibodies for ATPB, and NDUFS1, and with AP-conjugated secondary antibodies. Proteins were detected by BCIP/NBT method following the instruction for the Western blot kit.

Statistical analysis

Electrocardiogram data were expressed as mean \pm standard error (SE). Two-way ANOVA was used to test difference of basic parameters between groups. Independent sample *t*-test was used to estimate difference between groups, with $P < 0.05$ considered statistically significant. Analyses were performed with SPSS 17.0 (SPSS Inc., Chicago, IL, USA) software.

RESULTS

Effect of long-term Shenxianshengmai treatment on slow heart rate

Representative electrocardiography recordings of sham, model, and SXSM-treated rabbits are illustrated and analyzed in Figure 1 and Table 2, respectively. No difference was observed among baselines of all groups ($t = 1.459$, $P > 0.05$). As is evident, chemical injury of sinoatrial node decreased the mean heart rate by 32% (RR interval from 253 ± 10 ms in sham group to 406 ± 35 ms in model group, $t = 10.296$, $P < 0.05$, $n = 6$, respectively) after six weeks. This effect was partially reversed by 4-week SXSM treatment ($275 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$, RR interval from 406 ± 35 ms in model group to 251 ± 3 ms in M+SXSM group, $t = 10.491$, $P <$

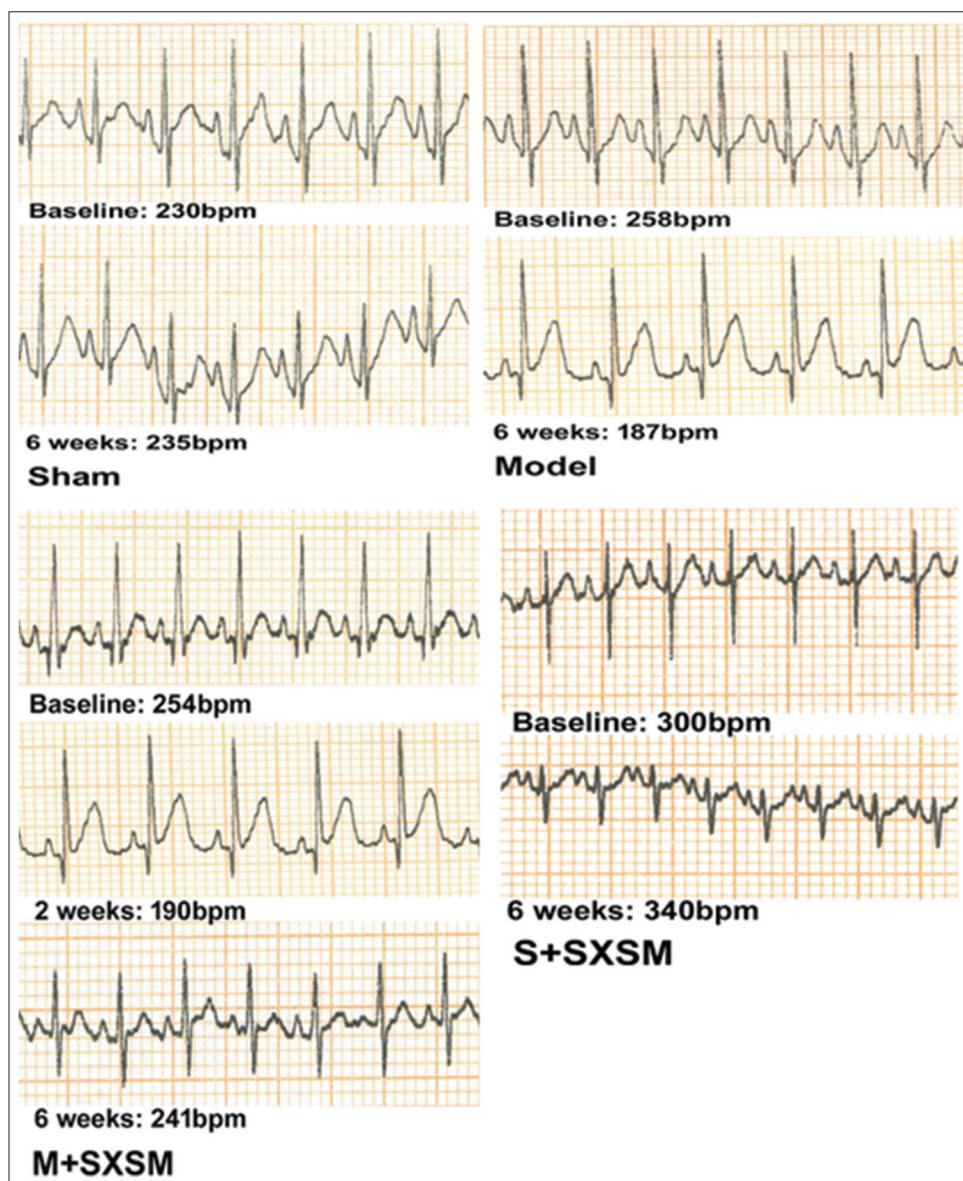


Figure 1: SXSM effects on cardiac electrical activity in anesthetized rabbits. Representative ECG recording (Lead II) obtained in one rabbit from sham (top-left), model (top-right), M+SXSM (bottom-left) and S+SXSM group (bottom-right) under baseline conditions (previous to operation) and after 2 weeks and 6 weeks of treatment. SXSM: Shenxianshengmai; S+SXSM: Sham plus SXSM; M+SXSM: Model plus SXSM; ECG: Electrocardiography; bpm: beats/min.

0.05). In addition, SXSM also increased heart rate of sham rabbits (RR interval from 406 ± 35 ms in model group to 186 ± 8 ms in S+SXSM group, $P < 0.05$). Except for RR interval, SXSM had no significant effect on atrial, atrioventricular, and ventricular conduction parameters, since the P, PR, QRS, and QT interval were not modified [Table 2].

Effects of long-term Shenxianshengmai treatment on cardiac transcripts

To explore the gene expression changes induced by chemical lesions of SA node, we compared sham and model group and identified 102 altered genes, among which 72 genes were downregulated and 30 were upregulated [Supplementary Table 1]. To follow the changes induced by SXSM treatment, we compared model and M+SXSM rabbits and found 109 differentially expressed genes [60 downregulated and 49 upregulated, Supplementary Table 2]. Among these altered genes, a total of 11 genes (ATP2A1, ERP27, FKBP1B, MBIP, PPIC, PRKCZ, VIPR1, PRLR, NIM1K, LOC100355813, and MMP1) were appeared in both model and SXSM originated differentially expressed genes [Supplementary Figure 1]. Moreover, the expressions of nine of them (ATP2A1, ERP27, FKBP1B, MBIP, PPIC, PRKCZ, VIPR1, PRLR, and NIM1K) were restored by SXSM in model rabbits [Table 1].

Our results revealed that SXSM increased heart rate by inhibiting heart parasympathetic transmission based on

the decreased CHRNA2 (encodes nicotinic acetylcholine receptor) and increased ACE-1 (encodes acetylcholinesterase) [Table 1]. They all indicate that parasympathetic synaptic transmission in heart was inhibited by SXSM. Therefore, sympathetic nerve was relatively stimulated and the heart rate increased.

In addition, restored calcium handling also plays an essential role in the increased heartbeat. Both ATP2A1 (encodes calcium ATPase, SERCA2a) and FKBP1B (encodes FKBP12.6 protein, an inhibitor of calcium release channel [RyR2]) were downregulated in model group and upregulated in M+SXSM group. Therefore, restored Ca^{2+} stores induced by restored expression of ATP2A1 and FKBP1B contribute directly to the increased heart rate through functioning similarly to sympathetic stimulation.

Restored signaling also plays an important role in the effect of SXSM due to the restored MBIP, PPIC, PRKCZ, vasoactive intestinal peptide receptor (VIPR), PRLR.

Confirmation of altered gene expression by quantitative real-time reverse transcription-polymerase chain reaction

Quantitative real-time RT-PCR was performed to confirm the results from gene expression chip. Four altered genes – ATP2A1, ERP27, FKBP1B, and MBIP – were selected. The relative mRNA expression level of each selected gene was

Table 2: ECG parameters in anesthetized rabbit from sham, control and SXSM before and after treatment groups

Groups	RR (ms)		P (ms)		PR (ms)		QRS (ms)		QT (ms)		QTc (ms)	
	Baseline	Week 6	Baseline	Week 6	Baseline	Week 6	Baseline	Week 6	Baseline	Week 6	Baseline	Week 6
Sham	246 ± 10	253 ± 10	40 ± 0	40 ± 0	63 ± 3	63 ± 3	23 ± 3	23 ± 3	160 ± 4	170 ± 4	102 ± 3	103 ± 2
Model	241 ± 10	406 ± 35*	40 ± 0	40 ± 0	62 ± 1	60 ± 0	21 ± 1	25 ± 3	163 ± 3	185 ± 11	105 ± 2	93 ± 6
M+SXSM	226 ± 8	251 ± 3†	40 ± 0	40 ± 0	60 ± 0	61 ± 1	20 ± 2	21 ± 3	153 ± 4	160 ± 2	101 ± 1	101 ± 1
S+SXSM	235 ± 3	186 ± 8*	40 ± 0	38 ± 2	60 ± 0	58 ± 1	26 ± 4	20 ± 1	156 ± 2	140 ± 0	103 ± 1	103 ± 2

* $P < 0.01$, model/S + SXSM versus sham group; † $P < 0.01$, M+SXSM versus model group. Data expressed as mean ± SE. $n = 6$ in each group. ECG parameters obtained in anesthetized rabbit from sham, model, M+SXSM and S+SXSM groups before treatment (baseline) and after 6 weeks of treatment. RR: RR interval; P: P wave duration; PQ: PQ interval; QRS: QRS complex duration; QT: QT interval; QTc: Corrected QT interval. $QTc = QT/2\sqrt{RR/100}$; SEM: Standard error of mean; ECG: Electrocardiogram; SXSM: Shenxianshengmai; M+SXSM: Model plus Shenxianshengmai; S+SXSM: Sham plus Shenxianshengmai.

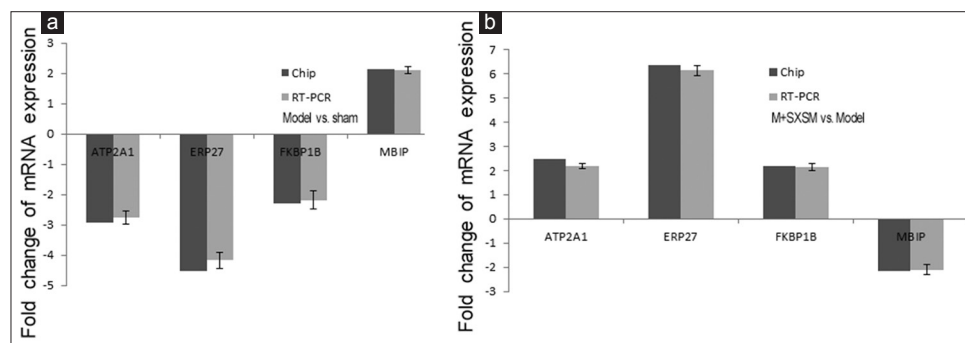


Figure 2: Confirmation of altered gene expression by quantitative real-time RT-PCR. (a) ATP2A1, ERP27, and FKBP1B were increased while MBIP was reduced in model vs. sham group according to real-time RT-PCR. (b) ATP2A1, ERP27, and FKBP1B were down-regulated while MBIP was upregulated in M+SXSM versus model group according to real-time RT-PCR. The relative mRNA expression level of each gene was normalized to 18S rRNA. The mRNA expression trends from real-time RT-PCR were in agreement with gene expression chip. RT-PCR: Reverse transcription-polymerase chain reaction; M+SXSM: Model plus Shenxianshengmai.

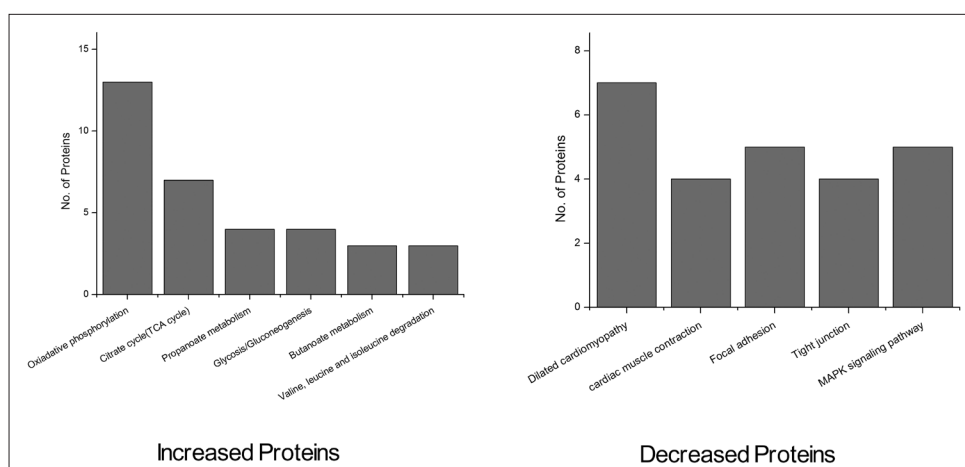


Figure 3: Altered proteins in ventricular myocardium after SXSM treatment. The most altered proteins were those participate in oxidative phosphorylation and TCA cycle. SXSM: Shenxianshengmai; TCA: Tricarboxylic acid.

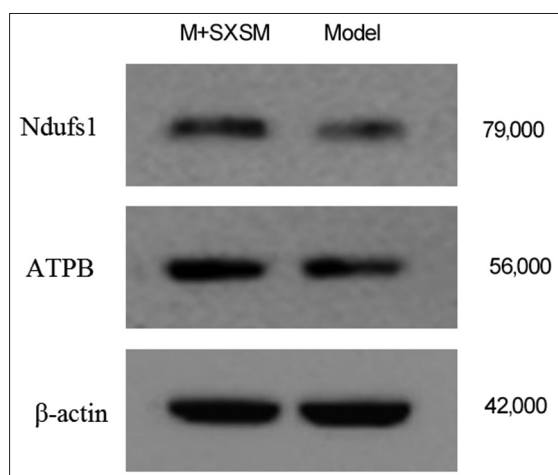


Figure 4: Expression of ATP synthase subunit beta (encoding by ATP5B) and complex I subunit (encoding by NDUFS1) after SXSM treatment by Western blotting. β -actin was used as the internal protein. The results of Western blotting were from a representative of three repeated experiments. SXSM: Shenxianshengmai.

normalized to 18S rRNA. As demonstrated in Figure 2, the expression trend of mRNA expression changes as verified by real-time RT-PCR was in agreement with that detected by gene expression chip.

Effects of long-term Shenxianshengmai treatment on cardiac proteins

A total of 125 proteins were altered after SXSM treatment [Supplementary Table 3]. As displayed in Figure 3, the most altered proteins were those participate in oxidative phosphorylation and tricarboxylic acid (TCA) cycle. SXSM-enhanced TCA cycle due to increased aconitate hydratase, succinyl-CoA ligase (GDP-forming) subunit alpha and beta (SUCLG1/2) and succinyl-CoA ligase (ADP-forming) subunit beta (SUCLGA2), isocitrate dehydrogenase2, and dihydrolipoyllysine-residue acetyltransferase component of pyruvate dehydrogenase complex (DLAT, PDHB). SXSM also increased NADH dehydrogenase. The upregulated proteins include NADH dehydrogenase (complex I)

core subunit (NDUFS1/3, NDUFV2), accessory subunit (NDUFS4/5), alpha (NDUFA2/7/8/9/12/13), and beta (NDUFB6) subcomplex. In addition, two subunits of mitochondrial ATP synthase (encoded by ATP5B and ATP5H) were also increased. These increased proteins may lead to enhanced mitochondrial membrane respiratory chain and increased ATP generation. All these results demonstrated that SXSM could improve the energy supplement of ventricular myocardium.

Confirmation of altered proteins by Western blot

Western blot was performed to confirm the results from iTRAQ. Considering the biological function, we selected two increased proteins: ATP synthase subunit beta (encoding by ATP5B) and complex I subunit (encoding by NDUFS1). β -actin was also detected as an internal control. As demonstrated in Figure 4, beta subunit of ATP synthase and subunit of complex I also increased after four weeks treatment with SXSM. This result was in agreement with that detected by iTRAQ.

DISCUSSION

The present study shows directly or indirectly mRNA remodeling of bradycardia for the first time and demonstrates that SXSM is effective in treating bradycardia. However, it is not possible to assume that all changes in gene expression are coupled to the development of bradycardia. In fact, the present data did not exclude the possibility that the part of the gene expression modifications was associated with the SA lesion, or secondary to the development of bradycardia.

Our results revealed that SXSM increased heart rate by inhibiting heart parasympathetic transmission based on the decreased CHRNA2 (encodes nicotinic acetylcholine receptor) and increased ACE-1 (encodes acetylcholinesterase). Reduced nicotinic acetylcholine receptors (encoded by CHRNA2), which form acetylcholine (ACh)-gated ion channels on the presynaptic and postsynaptic sides of the neuromuscular junction,^[18] suggested the inhibition of heart parasympathetic transmission. Moreover, it is well known

that acetylcholinesterase (encoded by ACE-1) locates at mainly neuromuscular junctions and serves to terminate parasympathetic synaptic transmission by hydrolyzing the neurotransmitter ACh.^[13] The increased expression of ACE-1 after SXSM treatment also indicates that parasympathetic synaptic transmission in heart was inhibited by SXSM. Therefore, sympathetic nerve was relatively stimulated. In addition to an increased force of heartbeat, this stimulation also causes the increase in heart rate.^[14]

Moreover, restored calcium handling also plays an essential role in the increased heartbeat. Bramich *et al.* reported that increases in force and heart rate evoked by sympathetic nerve stimulation resulted from the release of Ca²⁺ from intracellular Ca²⁺ stores-endoplasmic reticulum (ER).^[14] FKBP12.6 inhibits basal RyR2 activity. PKA-dependent RyR2 phosphorylation interrupts FKBP12.6-RyR2 association and activates RyR2 in myocytes.^[22,23] Sarcoplasmic reticulum (SR)/ER calcium ATPases (SERCAs) are calcium pumps that couple ATP hydrolysis with calcium transport across the SR/ER membrane. As a consequence of this activity, they maintain a level of resting intra-ER free calcium that is three to four orders of magnitude higher than the cytosolic Ca²⁺ concentration.^[19] Reduced SR Ca²⁺ release is due to diminished SR Ca²⁺ content directly related to a depressed expression of SERCA2a protein. Enhancing SERCA2a expression may improve SR Ca²⁺ handling in failing human myocardium.^[20] From our results, both ATP2A1 and FKBP1B were downregulated in model group and upregulated in M+SXSM group. Therefore, restored Ca²⁺ stores induced by restored expression of SERCA2a and FKBP12.6 contributed directly to increased heart rate.

Previous studies suggested that reduced ACE (encodes angiotensin I converting enzyme) may contribute to the improvement of heart function.^[35] Hence, reduced ACE after SXSM treatment may also play a positive role in heart.

In addition, restored signaling also plays an important role in the effect of SXSM due to the restored MBIP, PPIC, PRKCZ, VIPR, and PRLR. MBIP interacts with MUK/DLK/ZPK (a MAPKKK class protein kinase) and inhibits the activity of it to induce JNK/SAPK activation.^[25] The protein encoded by PPIC is a member of the PPIase family. PPIases catalyze the *cis*-trans isomerization of proline imidic peptide bonds in oligopeptides and accelerate the folding of proteins.^[26] Along with PPIB, PPIC localizes to the ER, where it maintains redox homeostasis.^[27] Increasing evidence from studies using *in vitro* and *in vivo* systems points to PKC zeta (PRKCZ) as a key regulator of critical intracellular signaling pathways such as mitogen-activated protein kinase cascade, transcription factor nuclear factor-kappa B activation, ribosomal S6-protein kinase signaling, and cell polarity.^[28] VIPR is a receptor for vasoactive intestinal peptide. The activity of it is mediated by G proteins which activate adenylyl cyclase.^[29] The PRLR is a cytokine receptor, and second messenger cascades include the JAK-STAT pathway, JAK-RUSH pathway, Ras-Raf-MAPK, and PI3K/AKT/mTOR pathway.^[30]

In ventricular myocardium, SXSM increased the supply of ATP by enhancing TCA cycle and oxidation-respiratory chain. Upregulated proteins ranged from enzymes of TCA cycle to subunits of complex I and ATP synthase. It was well known that mitochondrial ATP synthase catalyzes ATP synthesis.^[36] It included two complexes: the soluble catalytic core, F1, and the membrane-spanning component, F0, which comprises the proton channel. The F1 complex consists of 5 different subunits (alpha, beta, gamma, delta, and epsilon). The F0 seems to have nine subunits (a, b, c, d, e, f, g, and F6 and 8).^[37] According to our results, the increased ATP5B and ATP5H encode the beta subunit of F1 and d subunit of the F0 complex, respectively. Thus, ATP generation was effectively enhanced in ventricular myocardium.

In conclusion, our bradycardia model showed that long-term SXSM stimulates sympathetic transmission by increasing the expression of acetylcholinesterase and reduces the expression of nicotinic receptor to increase heart rate. SXSM also restored the calcium handling genes and altered genes involved in signaling. In addition, SXSM improves the ATP supply of ventricular myocardium by increasing proteins involved in TCA cycle and oxidation-respiratory chain. These data provide insights for the future study of SXSM.

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Supplementary information is linked to the online version of the paper on the Chinese Medical Journal website.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Altered genes induced by chemical lesions of SA node

Probe name	P (model)	FC ([M-C] vs. [N-C])	Log FC ([M-C] vs. [N-C])	FC (abs) ([M-C] vs. [N-C])	Regulation ([M-C] vs. [N-C])	Gene symbol	Description
A_04_P050087	2.13E-04	-5.90264	-2.5613604	5.902604	Down	CDHR2	Cadherin-related family member 2 (source: HGNC symbol; Acc.: 18231) (ENSOCUT00000011957)
A_04_P087007	0.023285631	-3.5565941	-1.8304963	3.5565941	Down	NIM1K	NIM1 serine/threonine protein kinase (source: HGNC symbol; Acc.: 28646) (ENSOCUT00000017806)
A_04_P087010	0.028032145	-3.750003	-1.9068918	3.750003	Down	NIM1K	NIM1 serine/threonine protein kinase (source: HGNC symbol; Acc.: 28646) (ENSOCUT00000017806)
A_04_P087011	0.03808915	-3.5096507	-1.8113275	3.5096507	Down	NIM1K	NIM1 serine/threonine protein kinase (source: HGNC symbol; Acc.: 28646) (ENSOCUT00000017806)
A_04_P079903	0.028085012	-4.738601	-2.2444613	4.738601	Down	SLCO6A1	Solute carrier organic anion transporter family, member 6A1 (source: HGNC symbol; Acc.: 23613) (ENSOCUT00000003395)
A_04_P016633	0.003186869	-2.1107936	-1.0777855	2.1107936	Down	PPARA	<i>O. cuniculus</i> mRNA for peroxisome proliferator-activated receptor alpha, partial (Y16420)
A_04_P000252	0.022043498	-2.3649971	-1.2418385	2.3649971	Down	SLC17A1	<i>O. cuniculus</i> solute carrier family 17 (organic anion transporter), member 1 (SLC17A1), mRNA (NM_001082307)
A_04_P087112	0.037798274	-2.2228696	-1.1524234	2.2228696	Down	GALNT6	GalNAc-T6 (source: HGNC symbol; Acc.: 4128) (ENSOCUT00000016142)
A_04_P060083	0.033848617	-2.0396495	-1.0283213	2.0396495	Down	FAM46A	Predicted: <i>O. cuniculus</i> FAM46A, transcript variant X1, mRNA (XM_002714547)
A_04_P070742	0.011976678	-2.6385913	-1.3997679	2.6385913	Down	LEPRE1	Leucine proline-enriched proteoglycan (leprecan) 1 (source: HGNC symbol; Acc.: 19316) (ENSOCUT00000005604)
A_04_P003811	0.018036077	-2.2830641	-1.1909714	2.2830641	Down	POMC	Predicted: <i>O. cuniculus</i> POMC, mRNA (XM_008254814)
A_04_P100217	0.012590322	-2.6345034	-1.397531	2.6345034	Down	UNC5C	unc-5 homolog C (<i>C. elegans</i>) (source: HGNC symbol; Acc.: 2569) (ENSOCUT000000027103)
A_04_P034932	0.03228504	-2.4518998	-1.2939	2.4518998	Down	CYGB	Cytoglobin (source: HGNC symbol; Acc.: 16505) (ENSOCUT00000007189)
A_04_P002327	0.020543803	-3.3467507	-1.7427611	3.3467507	Down	CRP	<i>O. cuniculus</i> CRP, pentraxin-related, mRNA (NM_001082265)
A_04_P089645	0.041924737	-2.2000206	-1.137517	2.2000206	Down	PSD3	Pleckstrin and Sec7 domain containing 3 (source: HGNC symbol; Acc.: 19093) (ENSOCUT000000025561)
A_04_P017086	0.044797514	-3.5483832	-1.8271618	3.5483832	Down	SERPINF1	Serpin peptidase inhibitor, clade F (alpha-2 antiplasmin, pigment epithelium derived factor), member 1 (source: HGNC symbol; Acc.: 8824) (ENSOCUT00000000092)

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Supplementary Table 1: Contd...

Probe name	P (model)	FC ([M-C] vs. [N-C])	Log FC ([M-C] vs. [N-C])	FC (abs) ([M-C] vs. [N-C])	Regulation ([M-C] vs. [N-C])	Gene symbol	Description
A_04_P089643	0.029146606	-2.290933	-1.1959352	2.290933	Down	PSD3	Pleckstrin and Sec7 domain containing 3 (source: HGNC symbol; Acc.: 19093) (ENSOCUT00000025561)
A_04_P093249	0.039436527	-2.9985077	-1.5842447	2.9985077	Down	MMP2	<i>O. cuniculus</i> MMP2 (gelatinase A, 72 kDa gelatinase, 72 kDa Type IV collagenase) (MMP2), mRNA (NM_001082209)
A_04_P051682	0.015472568	-6.1579328	-2.622446	6.1579328	Down	MFAP5	Microfibrillar associated protein 5 (source: HGNC symbol; Acc.: 29673) (ENSOCUT00000002406)
A_04_P089644	0.036751527	-2.12099	-1.0847378	2.12099	Down	PSD3	Pleckstrin and Sec7 domain containing 3 (source: HGNC symbol; Acc.: 19093) (ENSOCUT00000025561)
A_04_P089642	0.030870933	-2.178746	-1.123498	2.178746	Down	PSD3	Pleckstrin and Sec7 domain containing 3 (source: HGNC symbol; Acc.: 19093) (ENSOCUT00000025561)
A_04_P089646	0.04265277	-2.2121258	-1.1454334	2.2121258	Down	PSD3	Pleckstrin and Sec7 domain containing 3 (source: HGNC symbol; Acc.: 19093) (ENSOCUT00000025561)
A_04_P072427	0.028034508	-5.3536167	-2.4205139	5.3536167	Down	ERP27	Endoplasmic reticulum protein 27 (source: HGNC symbol; Acc.: 26495) (ENSOCUT0000006001)
A_04_P093247	0.041405607	-2.8864455	-1.529294	2.8864455	Down	MMP2	<i>O. cuniculus</i> MMP2 (gelatinase A, 72 kDa gelatinase, 72 kDa Type IV collagenase) (MMP2), mRNA (NM_001082209)
A_04_P093248	0.043032378	-2.7668319	-1.468235	2.7668319	Down	MMP2	<i>O. cuniculus</i> MMP2 (gelatinase A, 72 kDa gelatinase, 72 kDa Type IV collagenase) (MMP2), mRNA (NM_001082209)
A_04_P004291	0.015457233	-2.0878642	-1.0620279	2.0878642	Down	PPIC	Peptidylprolyl isomerase C (cyclophilin C) (source: HGNC symbol; Acc.: 9256) (ENSOCUT00000012051)
A_04_P093251	0.039674506	-2.8214786	-1.4964514	2.8214786	Down	MMP2	<i>O. cuniculus</i> MMP2 (gelatinase A, 72 kDa gelatinase, 72 kDa Type IV collagenase), mRNA (NM_001082209)
A_04_P001576	0.00394646	-2.9770167	-1.5738673	2.9770167	Down	PRLR	<i>O. cuniculus</i> PRLR, mRNA (NM_001082231)
A_04_P088597	0.02296636	-3.065462	-1.6161046	3.065462	Down	TIAM1	T-cell lymphoma invasion and metastasis 1 (source: HGNC symbol; Acc.: 11805) (ENSOCUT00000016533)
A_04_P001881	0.023102732	-2.0472045	-1.0336552	2.0472045	Down	LPXN	<i>O. cuniculus</i> LPXN, mRNA (NM_001082048)
A_04_P097699	0.001263165	-2.246798	-1.1678705	2.246798	Down	THSD7B	Thrombospondin, Type I, domain containing 7B (source: HGNC symbol; Acc.: 29348) (ENSOCUT00000004498)
A_04_P072428	0.038376957	-3.8443546	-1.9427414	3.8443546	Down	ERP27	Endoplasmic reticulum protein 27 (source: HGNC symbol; Acc.: 26495) (ENSOCUT0000006001)

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Supplementary Table 1: Contd...

Probe name	P (model)	FC ([M-C] vs. [N-C])	Log FC ([M-C] vs. [N-C])	FC (abs) ([M-C] vs. [N-C])	Regulation ([M-C] vs. [N-C])	Gene symbol	Description
A_04_P072431	0.04013448	-3.8216913	-1.9342113	3.8216913	Down	ERP27	Endoplasmic reticulum protein 27 (source: HGNC symbol; Acc.: 26495) (ENSOCUT00000006001)
A_04_P035132	0.044130646	-2.5600467	-1.3561702	2.5600467	Down	PLVAP	Plasmalemma vesicle associated protein (source: HGNC symbol; Acc.: 13635) (ENSOCUT00000016885)
A_04_P006131	0.009948871	-4.4479394	-2.1531372	4.4479394	Down	COL3A1	Collagen, Type III, alpha 1 (source: HGNC symbol; Acc.: 2201) (ENSOCUT00000015004)
A_04_P045978	0.031028168	-2.5334647	-1.3411117	2.5334647	Down	LOC100348745	Uncharacterized protein (source: UniProtKB/ TrEMBL; Acc.: G1TW35) (ENSOCUT00000022052)
A_04_P072429	0.039589465	-3.929553	-1.9743652	3.929553	Down	ERP27	Endoplasmic reticulum protein 27 (source: HGNC symbol; Acc.: 26495) (ENSOCUT00000006001)
A_04_P056432	0.03142421	-4.6996303	-2.2325473	4.6996303	Down	STAC2	SH3 and cysteine rich domain 2 (source: HGNC symbol; Acc.: 23990) (ENSOCUT00000014912)
A_04_P102148	0.018136093	-2.338483	-1.2255731	2.338483	Down	LOC100348745	Uncharacterized protein (source: UniProtKB/ TrEMBL; Acc.: G1TW35) (ENSOCUT00000022052)
A_04_P082384	0.047478992	-2.9464633	-1.5589843	2.9464633	Down	LOC100354746	L-3-hydroxyproline dehydratase (trans-) (source: HGNC symbol; Acc.: 20488) (ENSOCUT00000013400)
A_04_P033409	0.003330424	-2.0835822	-1.059066	2.0835822	Down	CCNE2	Cyclin E2 (source: UniProtKB/ TrEMBL; Acc.: A8UKE8) (ENSOCUT00000005398)
A_04_P038492	0.010132602	-2.2381797	-1.1623259	2.2381797	Down	DUSP21	Dual specificity phosphatase 21 (source: HGNC symbol; Acc.: 20476) (ENSOCUT00000009967)
A_04_P058592	0.040390886	-2.7010481	-1.4335194	2.7010481	Down	GPX7	<i>O. cuniculus</i> GPX7, mRNA (NM_001256904)
A_04_P059827	0.01597391	-2.5964324	-1.3765306	2.5964324	Down	LOC100340044	Nephronophthisis 4 (source: HGNC symbol; Acc.: 19104) (ENSOCUT00000002222)
A_04_P095797	0.03869427	-6.470327	-2.6938386	6.470327	Down	NDUFAF2	NADH dehydrogenase (ubiquinone) complex I, assembly factor 2 (source: HGNC symbol; Acc.: 28086) (ENSOCUT00000004524)
A_04_P095799	0.03740461	-6.1531677	-2.6213293	6.1531677	Down	NDUFAF2	NADH dehydrogenase (ubiquinone) complex I, assembly factor 2 (source: HGNC symbol; Acc.: 28086) (ENSOCUT00000004524)
A_04_P099602	0.015056029	-3.599814	-1.8479223	3.599814	Down	COL3A1	Collagen, Type III, alpha 1 (source: HGNC symbol; Acc.: 2201) (ENSOCUT00000015004)
A_04_P099603	0.020265575	-3.3484626	-1.7434988	3.3484626	Down	COL3A1	Collagen, Type III, alpha 1 (source: HGNC symbol; Acc.: 2201) (ENSOCUT00000015004)

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Supplementary Table 1: Contd...

Probe name	P (model)	FC ([M-C] vs. [N-C])	Log FC ([M-C] vs. [N-C])	FC (abs) ([M-C] vs. [N-C])	Regulation ([M-C] vs. [N-C])	Gene symbol	Description
A_04_P092587	0.036181234	-2.9673595	-1.5691798	2.9673595	Down	ANLN	Predicted: <i>O. cuniculus</i> anillin, actin binding protein (ANLN), transcript variant X4, mRNA (XM_008261645)
A_04_P054449	0.01497467	-2.6039603	-1.3807075	2.6039603	Down	MMP1	<i>O. cuniculus</i> MMP1 (interstitial collagenase), mRNA (NM_001171139)
A_04_P083948	0.03093418	-2.1244	-1.0870554	2.1244	Down	LOC100358172	Uncharacterized protein (source: UniProtKB/TrEMBL; Acc.: G1TBJ2) (ENSOCUT00000016394)
A_04_P099605	0.019832825	-3.3901873	-1.7613649	3.3901873	Down	COL3A1	Collagen, Type III, alpha 1 (source: HGNC symbol; Acc.: 2201) (ENSOCUT00000015004)
A_04_P033287	0.01829139	-2.8958638	-1.5339937	2.8958638	Down	COL1A2	<i>O. cuniculus</i> COL1A2, mRNA (NM_001195668)
A_04_P029302	0.02377222	-3.152118	-1.6563215	3.152118	Down	COL3A1	Collagen, Type III, alpha 1 (Source: HGNC symbol; Acc.: 2201) (ENSOCUT00000015004)
A_04_P061512	0.04516693	-2.5043848	-1.3244562	2.5043848	Down	ECM2	Extracellular matrix protein 2, female organ and adipocyte specific (source: HGNC symbol; Acc.: 3154) (ENSOCUT00000008293)
A_04_P003721	0.021280957	-5.6962433	-2.5100107	5.6962433	Down	COL1A1	nbc40c08.y1 Rabbit trigeminal nerve. Unnormalized (nbc) <i>O. cuniculus</i> cDNA clone nbc40c08 5', mRNA sequence (EB378353)
A_04_P013577	0.042669218	-2.1812866	-1.1251793	2.1812866	Down	SLC4A7	<i>O. cuniculus</i> SLC4A7, mRNA (NM_001195836)
A_04_P053222	0.001118318	-2.0266144	-1.0190716	2.0266144	Down	LOC100356056	Olfactory receptor, family 5, subfamily K, member 3 (source: HGNC symbol; Acc.: 31290) (ENSOCUT00000021390)
A_04_P004432	0.019337988	-5.1568594	-2.3664927	5.1568594	Down	GSTM2	<i>O. cuniculus</i> glutathione S-transferase mu 2 (muscle) (GSTM2), mRNA (NM_001082252)
A_04_P099604	0.03374342	-2.9723594	-1.5716085	2.9723594	Down	COL3A1	Collagen, Type III, alpha 1 (source: HGNC symbol; Acc.: 2201) (ENSOCUT00000015004)
A_04_P097917	0.014595655	-2.363482	-1.2409139	2.363482	Down	DNAH11	Dynein, axonemal, heavy chain 11 (source: HGNC symbol; Acc.: 2942) (ENSOCUT00000014002)
A_04_P067988	0.025094591	-2.113492	-1.0796286	2.113492	Down	POLQ	Polymerase (DNA directed), theta (source: HGNC symbol; Acc.: 9186) (ENSOCUT00000008087)
A_04_P080226	0.04116367	-2.2043643	-1.1403627	2.2043643	Down	FAS	<i>O. cuniculus</i> Fas cell surface death receptor (FAS), mRNA (NM_001081995)
A_04_P005106	0.029306017	-3.483605	-1.800581	3.483605	Down	COL1A2	<i>O. cuniculus</i> COL1A2, mRNA (NM_001195668)
A_04_P080223	0.017979171	-2.6730063	-1.4184632	2.6730063	Down	FAS	<i>O. cuniculus</i> Fas cell surface death receptor (FAS), mRNA (NM_001081995)

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Supplementary Table 1: Contd...

Probe name	P (model)	FC ([M-C] vs. [N-C])	Log FC ([M-C] vs. [N-C])	FC (abs) ([M-C] vs. [N-C])	Regulation ([M-C] vs. [N-C])	Gene symbol	Description
A_04_P075839	0.04102744	-2.7049184	-1.435585	2.7049184	Down	KDELR3	KDEL (Lys-Asp-Glu-Leu) endoplasmic reticulum protein retention receptor 3 (source: HGNC symbol; Acc.:6306) (ENSOCUT00000004978)
A_04_P080225	0.047294028	-2.5963895	-1.3765068	2.5963895	Down	FAS	<i>O. cuniculus</i> Fas cell surface death receptor (FAS), mRNA (NM_001081995)
A_04_P002113	0.002724072	-2.9282255	-1.5500267	2.9282255	Down	ATP2A1	<i>O. cuniculus</i> ATPase, Ca ⁺⁺ transporting, cardiac muscle, fast twitch 1 (ATP2A1), mRNA (NM_001089318)
A_04_P075838	0.04812213	-2.6296778	-1.394886	2.6296778	Down	KDELR3	KDEL (Lys-Asp-Glu-Leu) endoplasmic reticulum protein retention receptor 3 (source: HGNC symbol; Acc.: 6306) (ENSOCUT00000004978)
A_04_P083155	0.027226511	-3.4746482	-1.7968669	3.4746482	Down	FGF12	Fibroblast growth factor 12 (source: HGNC symbol; Acc.: 3668) (ENSOCUT00000007581)
A_04_P095802	0.035368208	-2.8162816	-1.4937916	2.8162816	Down	TP63	Tumor protein p63 (source: HGNC symbol; Acc.: 15979) (ENSOCUT00000016469)
A_04_P029967	0.027289847	-3.2396457	-1.6958361	3.2396457	Down	COL1A2	<i>O. cuniculus</i> COL1A2, mRNA (NM_001195668)
A_04_P051867	0.026114652	-4.3361998	-2.1164312	4.3361998	Down	KAZALD1	Kazal-type serine peptidase inhibitor domain 1 (source: HGNC symbol; Acc.: 25460) (ENSOCUT00000002973)
A_04_P005011	0.027014492	-2.4109325	-1.2695913	2.4109325	Down	SPARC	SPARC (source: UniProtKB/Swiss-Prot; Acc.: P36233) (ENSOCUT00000012119)
A_04_P007976	0.047936346	-2.7027574	-1.434432	2.7027574	Down	FBN1	Fibrillin 1 (source: HGNC symbol; Acc.: 3603) (ENSOCUT00000033355)
A_04_P080222	0.04711833	-2.5315278	-1.3400083	2.5315278	Down	FAS	<i>O. cuniculus</i> FAS death receptor, mRNA (NM_001081995)
A_04_P005107	0.03109285	-3.681179	-1.880168	3.681179	Down	COL1A2	<i>O. cuniculus</i> COL1A2, mRNA (NM_001195668)
A_04_P092167	0.02343565	-3.664335	-1.8735514	3.664335	Down	PDLIM3	PDZ and LIM domain 3 (source: HGNC symbol; Acc.: 20767) (ENSOCUT00000005808)
A_04_P016398	0.024049735	-2.2937021	-1.1976781	2.2937021	Down	FKBP1B	nbc39d02.x1 Rabbit trigeminal nerve. Unnormalized (nbc) <i>O. cuniculus</i> cDNA clone nbc39d02 3', mRNA sequence (EB378230)
A_04_P083153	0.02726263	-3.4423661	-1.7834005	3.4423661	Down	FGF12	Fibroblast growth factor 12 (source: HGNC symbol; Acc.: 3668) (ENSOCUT00000007581)
A_04_P005109	0.0369753	-3.5455344	-1.8260031	3.5455344	Down	COL1A2	<i>O. cuniculus</i> COL1A2, mRNA (NM_001195668)
A_04_P033295	0.03675723	-3.8002567	-1.9260969	3.8002567	Down	COL1A2	<i>O. cuniculus</i> COL1A2, mRNA (NM_001195668)
A_04_P033296	0.031819753	-3.8275986	-1.9364395	3.8275986	Down	COL1A2	<i>O. cuniculus</i> COL1A2, mRNA (NM_001195668)
A_04_P033663	0.002227771	-2.3468587	-1.230731	2.3468587	Down	LOC100356573	PREDICTED: <i>O. cuniculus</i> olfactory receptor 183-like (LOC100356573), mRNA (XM_008267070)

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Supplementary Table 1: Contd...

Probe name	P (model)	FC ([M-C] vs. [N-C])	Log FC ([M-C] vs. [N-C])	FC (abs) ([M-C] vs. [N-C])	Regulation ([M-C] vs. [N-C])	Gene symbol	Description
A_04_P033294	0.031522974	-3.9890788	-1.9960556	3.9890788	Down	COL1A2	<i>O. cuniculus</i> COL1A2, mRNA (NM_001195668)
A_04_P033293	0.030434528	-3.9730337	-1.990241	3.9730337	Down	COL1A2	<i>O. cuniculus</i> COL1A2, mRNA (NM_001195668)
A_04_P083152	0.026679767	-3.68019	-1.8797803	3.68019	Down	FGF12	Fibroblast growth factor 12 (source: HGNC symbol; Acc.:3668) (ENSOCUT00000007581)
A_04_P034532	0.011843006	-2.131761	-1.0920458	2.131761	Down	LOC100355813	Predicted: <i>O. cuniculus</i> putative olfactory receptor GPCRLTM7 (LOC100355813), mRNA (XM_008269585)
A_04_P033292	0.032284934	-3.7423513	-1.903945	3.7423513	Down	COL1A2	<i>O. cuniculus</i> COL1A2, mRNA (NM_001195668)
A_04_P041922	0.035629585	-2.813322	-1.4922748	2.813322	Down	BEX4	Brain expressed, X-linked 4 (source: HGNC symbol; Acc.: 25475) (ENSOCUT00000000444)
A_04_P041923	0.039250128	-3.5689461	-1.8354981	3.5689461	Down	BEX4	Brain expressed, X-linked 4 (source: HGNC symbol; Acc.: 25475) (ENSOCUT00000000444)
A_04_P083154	0.02627617	-3.6316636	-1.8606305	3.6316636	Down	FGF12	Fibroblast growth factor 12 (source: HGNC symbol; Acc.: 3668) (ENSOCUT00000007581)
A_04_P100467	0.037227023	-2.2789202	-1.1883504	2.2789202	Down	PPFIA2	Predicted: <i>O. cuniculus</i> PTPRF, interacting protein (liprin), PPFIA2, mRNA (XM_008256846)
A_04_P028651	0.028550228	-2.975188	-1.5729809	2.975188	Down	CCDC80	Coiled-coil domain containing 80 (source: HGNC symbol; Acc.: 30649) (ENSOCUT00000022757)
A_04_P005108	0.040823817	-3.2330394	-1.6928911	3.2330394	Down	COL1A2	<i>O. cuniculus</i> COL1A2, mRNA (NM_001195668)
A_04_P036902	0.04764918	-3.0791728	-1.6225429	3.0791728	Down	ANGPTL4	Angiopoietin-like 4 (source: HGNC symbol; Acc.: 16039) (ENSOCUT00000016598)
A_04_P082732	0.04945613	-2.3887203	-1.256238	2.3887203	Down	CBR3	Carbonyl reductase 3 (source: HGNC symbol; Acc.: 1549) (ENSOCUT00000016753)
A_04_P080444	0.01253518	-2.367927	-1.2436247	2.367927	Down	ITIH5	Inter-alpha-trypsin inhibitor heavy chain family, member 5 (source: HGNC symbol; Acc.: 21449) (ENSOCUT00000016950)
A_04_P080443	0.01416163	-2.3782194	-1.2498817	2.3782194	Down	ITIH5	Inter-alpha-trypsin inhibitor heavy chain family, member 5 (source: HGNC symbol; Acc.: 21449) (ENSOCUT00000016950)
A_04_P089937	0.012976293	-5.5949855	-2.4841344	5.5949855	Down	LOC100346910	Cytochrome P450, family 26, subfamily A, polypeptide 1 (source: HGNC symbol; Acc.: 2603) (ENSOCUT00000000178)
A_04_P000416	0.027141394	-2.9160402	-1.5440106	2.9160402	Down	SLC5A11	<i>O. cuniculus</i> solute carrier family 5 (sodium/inositol cotransporter), member 11 (SLC5A11), mRNA (NM_001082193)

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Supplementary Table 1: Contd...

Probe name	P (model)	FC ([M-C] vs. [N-C])	Log FC ([M-C] vs. [N-C])	FC (abs) ([M-C] vs. [N-C])	Regulation ([M-C] vs. [N-C])	Gene symbol	Description
A_04_P080445	0.013871072	-2.3409014	-1.2270641	2.3409014	Down	ITIH5	Inter-alpha-trypsin inhibitor heavy chain family, member 5 (source: HGNC symbol; Acc.: 21449) (ENSOCUT00000016950)
A_04_P089787	0.033155497	-2.0099761	-1.0071783	2.0099761	Down	CTTNBP2	<i>O. cuniculus</i> CTTNBP2, mRNA (NM_001171037)
A_04_P069826	0.00699335	-2.9462788	-1.5588939	2.9462788	Down	C16H1orf100	Predicted: <i>O. cuniculus</i> chromosome 16 open reading frame, human C1orf100 (C16H1orf100), mRNA (XM_008268175)
A_04_P080446	0.010715441	-2.386099	-1.2546539	2.386099	Down	ITIH5	Inter-alpha-trypsin inhibitor heavy chain family, member 5 (source: HGNC symbol; Acc.: 21449) (ENSOCUT00000016950)
A_04_P098652	0.036045354	-2.3227742	-1.2158489	2.3227742	Down	LOXL2	Lysyl oxidase-like 2 (source: HGNC symbol; Acc.: 6666) (ENSOCUT00000014596)
A_04_P057962	0.021160344	-2.3215833	-1.215109	2.3215833	Down	CREB3L1	cAMP responsive element binding protein 3-like 1 (source: HGNC symbol; Acc.: 18856) (ENSOCUT00000004418)
A_04_P035452	0.028131086	-2.155412	-1.1079636	2.155412	Down	ORYCUNV1R1649	<i>O. cuniculus</i> vomeronasal 1 receptor oryCunV1R1649 (ORYCUNV1R1649), mRNA (NM_001167331)
A_04_P069053	0.031732317	-2.417458	-1.2734909	2.417458	Down	ASXL3	Additional sex combs like 3 (<i>Drosophila</i>) (source: HGNC symbol; Acc.: 29357) (ENSOCUT00000021269)
A_04_P089791	0.028787576	-2.3628736	-1.2405424	2.3628736	Down	CTTNBP2	<i>O. cuniculus</i> CTTNBP2, mRNA (NM_001171037)
A_04_P069822	0.001974626	-2.0158546	-1.0113916	2.0158546	Down	C16H1orf100	Predicted: <i>O. cuniculus</i> chromosome 16 open reading frame, human C1orf100 (C16H1orf100), mRNA (XM_008268175)
A_04_P082177	0.026941413	-4.7234235	-2.2398329	4.7234235	Down	CHST9	Carbohydrate (N-acetylgalactosamine 4-0) sulfotransferase 9 (source: HGNC symbol; Acc.: 19898) (ENSOCUT00000004444)
A_04_P071528	0.045763444	-4.0166063	-2.0059772	4.0166063	Down	CXXC4	CXXC finger protein 4 (source: HGNC symbol; Acc.: 24593) (ENSOCUT00000015532)
A_04_P014266	0.009920757	-2.1841376	-1.1270638	2.1841376	Down	TH	<i>O. cuniculus</i> tyrosine hydroxylase mRNA, partial cds (AF493546)
A_04_P051042	0.024545448	2.8976667	1.5348916	2.8976667	Up	TMEM30B	Predicted: <i>O. cuniculus</i> TMEM30B, mRNA (XM_002719548)
A_04_P002301	0.01415297	2.115944	1.0813015	2.115944	Up	BCL2L1	<i>O. cuniculus</i> BCL2L1, mRNA (NM_001082135)
A_04_P027306	0.016862689	9.846998	3.299684	9.846998	Up	VIPR1	Uncharacterized protein (source: UniProtKB/TrEMBL; Acc.: G1T4R1) (ENSOCUT00000013108)
A_04_P068184	0.020826897	3.5468142	1.8265238	3.5468142	Up	PCBP3	Poly(rC) binding protein 3 (source: HGNC symbol; Acc.: 8651) (ENSOCUT00000002697)

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Supplementary Table 1: Contd...

Probe name	P (model)	FC ([M-C] vs. [N-C])	Log FC ([M-C] vs. [N-C])	FC (abs) ([M-C] vs. [N-C])	Regulation ([M-C] vs. [N-C])	Gene symbol	Description
A_04_P068182	0.02685825	2.9211617	1.5465422	2.9211617	Up	PCBP3	Poly(rC) binding protein 3 (source: HGNC symbol; Acc.:8651) (ENSOCUT00000002697)
A_04_P068183	0.017993355	3.245934	1.6986337	3.245934	Up	PCBP3	Poly(rC) binding protein 3 (source: HGNC symbol; Acc.: 8651) (ENSOCUT00000002697)
A_04_P040043	0.011545409	4.717317	2.2379665	4.717317	Up	IFIT1B	Predicted: <i>O. cuniculus</i> IFIT1B, transcript variant X2, mRNA (XM_008270168)
A_04_P027309	0.016133107	9.838605	3.2984538	9.838605	Up	VIPR1	Uncharacterized protein (source: UniProtKB/ TrEMBL; Acc.: G1T4R1) (ENSOCUT00000013108)
A_04_P068186	0.023552185	3.917972	1.9701071	3.917972	Up	PCBP3	Poly(rC) binding protein 3 (source: HGNC symbol; Acc.: 8651) (ENSOCUT00000002697)
A_04_P012977	0.02876307	2.6510959	1.4065888	2.6510959	Up	PPP2R2C	<i>O. cuniculus</i> protein phosphatase 2, regulatory subunit B, gamma (PPP2R2C), mRNA (NM_001171076)
A_04_P068185	0.029449334	3.7324986	1.9001417	3.7324986	Up	PCBP3	Poly(rC) binding protein 3 (source: HGNC symbol; Acc.: 8651) (ENSOCUT00000002697)
A_04_P003912	0.014354926	2.9154265	1.5437069	2.9154265	Up	SLC2A3	Solute carrier family 2, facilitated glucose transporter member 3 (source: UniProtKB/ TrEMBL; Acc.: G1TI27) (ENSOCUT00000024311)
A_04_P027307	0.022313578	7.3252916	2.8728862	7.3252916	Up	VIPR1	Uncharacterized protein (source: UniProtKB/ TrEMBL; Acc.: G1T4R1) (ENSOCUT00000013108)
A_04_P074137	0.028930737	4.79734	2.2622347	4.79734	Up	LOC100345657	DEAD (Asp-Glu-Ala-Asp) box polypeptide 60 (source: HGNC symbol; Acc.: 25942) (ENSOCUT00000006364)
A_04_P074138	0.03878298	4.2139044	2.0751576	4.2139044	Up	LOC100345657	DEAD (Asp-Glu-Ala-Asp) box polypeptide 60 (source: HGNC symbol; Acc.: 25942) (ENSOCUT00000006364)
A_04_P057689	0.031922758	2.0032291	1.0023274	2.0032291	Up	NOSTRIN	Nitric oxide synthase trafficking (source: HGNC symbol; Acc.: 20203) (ENSOCUT00000005730)
A_04_P040042	0.022928404	4.0235863	2.008482	4.0235863	Up	IFIT1B	Predicted: <i>O. cuniculus</i> IFIT1B, transcript variant X2, mRNA (XM_008270168)
A_04_P003626	0.04689884	2.6411679	1.401176	2.6411679	Up	PLA2G1B	Phospholipase A2, group IB (pancreas) (source: HGNC symbol; Acc.:9030) (ENSOCUT00000001103)
A_04_P027308	0.030365663	7.0353813	2.8146286	7.0353813	Up	VIPR1	Uncharacterized protein (source: UniProtKB/ TrEMBL; Acc.:G1T4R1) (ENSOCUT00000013108)

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Supplementary Table 1: Contd...

Probe name	P (model)	FC ([M-C] vs. [N-C])	Log FC ([M-C] vs. [N-C])	FC (abs) ([M-C] vs. [N-C])	Regulation ([M-C] vs. [N-C])	Gene symbol	Description
A_04_P027310	0.025073402	6.4645166	2.6925426	6.4645166	Up	VIPR1	Uncharacterized protein (source: UniProtKB/TrEMBL; Acc.: G1T4R1) (ENSOCUT00000013108)
A_04_P082358	0.011940352	2.7529871	1.4609978	2.7529871	Up	STAC	SH3 and cysteine rich domain (source: HGNC symbol; Acc.: 11353) (ENSOCUT00000014575)
A_04_P003914	0.026411507	2.3012784	1.2024355	2.3012784	Up	SLC2A3	Solute carrier family 2, facilitated glucose transporter member 3 (source: UniProtKB/TrEMBL; Acc.: G1TI27) (ENSOCUT00000024311)
A_04_P048467	0.006543531	12.897011	3.6889648	12.897011	Up	FABP2	Fatty acid binding protein 2, intestinal (source: HGNC symbol; Acc.: 3556) (ENSOCUT00000003292)
A_04_P098422	0.040197942	2.000406	1.0002928	2.000406	Up	EXOC4	Exocyst complex component 4 (source: HGNC symbol; Acc.: 30389) (ENSOCUT00000011683)
A_04_P101047	0.03208215	3.611811	1.8527224	3.611811	Up	SLC1A2	Solute carrier family 1 (glial high affinity glutamate transporter), member 2 (source: HGNC symbol; Acc.: 10940) (ENSOCUT00000000717)
A_04_P003913	0.015944535	2.813684	1.4924603	2.813684	Up	SLC2A3	Solute carrier family 2, facilitated glucose transporter member 3 (source: UniProtKB/TrEMBL; Acc.: G1TI27) (ENSOCUT00000024311)
A_04_P050054	0.010326308	2.1597826	1.1108861	2.1597826	Up	PPP1R8	Protein phosphatase 1, regulatory subunit 8 (source: HGNC symbol; Acc.: 9296) (ENSOCUT00000003550)
A_04_P050055	0.008846662	2.1733928	1.1199489	2.1733928	Up	PPP1R8	Protein phosphatase 1, regulatory subunit 8 (source: HGNC symbol; Acc.: 9296) (ENSOCUT00000003550)
A_04_P002261	0.022326231	3.2783065	1.7129507	3.2783065	Up	PRKCZ	<i>O. cuniculus</i> PRKCZ, mRNA (NM_001082758)
A_04_P050056	0.014406904	2.120411	1.0843439	2.120411	Up	PPP1R8	Protein phosphatase 1, regulatory subunit 8 (Source: HGNC symbol; Acc.:9296) (ENSOCUT00000003550)
A_04_P077452	0.041224316	2.3338618	1.2227192	2.3338618	Up	SOCS2	Predicted: <i>O. cuniculus</i> SOCS2, mRNA (XM_002711201)
A_04_P077456	0.046924546	2.2067058	1.1418943	2.2067058	Up	SOCS2	SOC2 (source: HGNC symbol; Acc.:19382) (ENSOCUT00000010933)
A_04_P077453	0.049324986	2.24936	1.1695147	2.24936	Up	SOCS2	Predicted: <i>O. cuniculus</i> SOCS2, mRNA (XM_002711201)
A_04_P002438	0.020600662	2.016859	1.0121102	2.016859	Up	STK17A	<i>O. cuniculus</i> STK17A, mRNA (NM_001082006)
A_04_P003915	0.031343848	2.1500535	1.1043725	2.1500535	Up	SLC2A3	Solute carrier family 2, facilitated glucose transporter member 3 (source: UniProtKB/TrEMBL; Acc.: G1TI27) (ENSOCUT00000024311)
A_04_P002437	0.011538388	2.0175784	1.0126247	2.0175784	Up	STK17A	<i>O. cuniculus</i> STK17A, mRNA (NM_001082006)

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Supplementary Table 1: Contd...

Probe name	P (model)	FC ([M-C] vs. [N-C])	Log FC ([M-C] vs. [N-C])	FC (abs) ([M-C] vs. [N-C])	Regulation ([M-C] vs. [N-C])	Gene symbol	Description
A_04_P001796	0.04731538	3.1353683	1.6486349	3.1353683	Up	CA4	<i>O. cuniculus</i> CA4, mRNA (NM_001082372)
A_04_P000366	0.04342749	2.741414	1.4549203	2.741414	Up	PGR	<i>O. cuniculus</i> PGR, mRNA (NM_001082267)
A_04_P092835	0.029530097	6.5730186	2.716556	6.5730186	Up	FGF16	Fibroblast growth factor 16 (source: HGNC symbol; Acc.: 3672) (ENSOCUT00000007573)
A_04_P092832	0.028704511	6.4459314	2.6883888	6.4459314	Up	FGF16	Fibroblast growth factor 16 (source: HGNC symbol; Acc.: 3672) (ENSOCUT00000007573)
A_04_P092834	0.030233566	6.420013	2.6825762	6.420013	Up	FGF16	Fibroblast growth factor 16 (source: HGNC symbol; Acc.: 3672) (ENSOCUT00000007573)
A_04_P084832	0.015358449	2.2615695	1.1773243	2.2615695	Up	MBIP	MAP3K12 binding inhibitory protein 1 (source: HGNC symbol; Acc.: 20427) (ENSOCUT00000017089)
A_04_P092833	0.02662034	6.495581	2.6994586	6.495581	Up	FGF16	Fibroblast growth factor 16 (source: HGNC symbol; Acc.: 3672) (ENSOCUT00000007573)
A_04_P000367	0.028090108	2.2779107	1.1877112	2.2779107	Up	PGR	<i>O. cuniculus</i> PGR, mRNA (NM_001082267)
A_04_P095007	0.033862874	2.7488995	1.4588542	2.7488995	Up	B3GAT2	Beta-1,3-glucuronyltransferase 2 (glucuronosyltransferase S) (source: HGNC symbol; Acc.: 922) (ENSOCUT00000017143)
A_04_P059047	0.011740238	2.0731213	1.0518045	2.0731213	Up	CD82	CD82 molecule (source: HGNC symbol; Acc.: 6210) (ENSOCUT00000000861)
A_04_P014040	0.023618352	2.205675	1.1412201	2.205675	Up	KCNE2	<i>O. cuniculus</i> KCNE2, mRNA (NM_001198937)
A_04_P068197	0.019358119	2.3287246	1.2195401	2.3287246	Up	ETV3L	ETS variant 3-like (source: HGNC symbol; Acc.: 33834) (ENSOCUT00000009586)
A_04_P084833	0.006848039	2.1374094	1.0958633	2.1374094	Up	MBIP	MAP3K12 binding inhibitory protein 1 (Source: HGNC symbol; Acc.: 20427) (ENSOCUT00000017089)
A_04_P084834	0.007091271	2.088237	1.0622854	2.088237	Up	MBIP	MAP3K12 binding inhibitory protein 1 (source: HGNC symbol; Acc.: 20427) (ENSOCUT00000017089)
A_04_P014038	0.006960096	2.1008282	1.0709581	2.1008282	Up	KCNE2	<i>O. cuniculus</i> KCNE2, mRNA (NM_001198937)
A_04_P071088	0.015779097	2.0521553	1.0371399	2.0521553	Up	CSF2	<i>O. cuniculus</i> CSF 2 (granulocyte-macrophage) mRNA (NM_001171257)
A_04_P003501	0.047569647	3.201583	1.6787853	3.201583	Up	S100A8	S100 calcium binding protein A8 (source: HGNC symbol; Acc.:10498) (ENSOCUT00000009566)
A_04_P035696	0.024071936	3.4406383	1.7826762	3.4406383	Up	TUBAL3	Tubulin, alpha-like 3 (source: HGNC symbol; Acc.: 23534) (ENSOCUT00000015599)
A_04_P013130	0.046058584	3.9531407	1.9829993	3.9531407	Up	S100A8	S100 calcium binding protein A8 (Source: HGNC symbol; Acc.: 10498) (ENSOCUT00000009566)

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Supplementary Table 1: Contd...

Probe name	P (model)	FC ([M-C] vs. [N-C])	Log FC ([M-C] vs. [N-C])	FC (abs) ([M-C] vs. [N-C])	Regulation ([M-C] vs. [N-C])	Gene symbol	Description
A_04_P013126	0.04638395	4.0099874	2.0035977	4.0099874	Up	S100A8	<i>O. cuniculus</i> mRNA for MRP-8, partial cds (D17405)
A_04_P003502	0.038870577	3.5022912	1.8082991	3.5022912	Up	S100A8	S100 calcium binding protein A8 (source: HGNC symbol; Acc.: 10498) (ENSOCUT00000009566)
A_04_P060934	0.014902458	2.02408	1.0172663	2.02408	Up	SLC17A5	<i>O. cuniculus</i> SLC17A5, mRNA (NM_001171293)
A_04_P003503	0.03559543	3.6532578	1.8691835	3.6532578	Up	S100A8	S100 calcium binding protein A8 (source: HGNC symbol; Acc.: 10498) (ENSOCUT00000009566)
A_04_P003505	0.0373169	3.538606	1.8231812	3.538606	Up	S100A8	S100 calcium binding protein A8 (source: HGNC Symbol; Acc.: 10498) (ENSOCUT00000009566)
A_04_P003504	0.0345601	3.7385707	1.9024868	3.7385707	Up	S100A8	S100 calcium binding protein A8 (source: HGNC symbol; Acc.: 10498) (ENSOCUT00000009566)

Probe name	Sequence
A_04_P050087	AAGTGGATTTCGTCTCTAAGGATGGGACCACATTGCCTTTGCAAAAACGCTTTTGAGATCC
A_04_P087007	AAGAAAAGGGTCCCGTGTCTACAGGGGCATAAGACACACGTCCAAATTTTGTTCATATTTA
A_04_P087010	AAGGGAAAGATGCTCGAAGCTCAATCACAGGGGTCTATAGAATCATTTTACATAGAGTCC
A_04_P087011	AGAACACATTCGAAATAATCAAGGGAAAGATGCTCGAAGCTCAATCACAGGGGTCTATAG
A_04_P079903	CTGTTGCATTTTATGTATATAAAGGTATTAGAAAGGAAAGCACTGAAAGCTTGCCATATGC
A_04_P016633	CAAGAGATCTACAGAGACATGACTGATTTTTCCCTGAGATGGTAGGCCGTTGCCACTGTT
A_04_P000252	TGGTTTTAAAATCTTCTCCTGATGCCATCATAATGTGATAAGCGTGATTTTCTACCTT
A_04_P087112	AAGATTTTCTACAGGAGAAATCTACAGGCAGCCAAGATGGCCCAAGAGAAATCCTTTGGG
A_04_P060083	AAGACAGACTTTAAATCTTATCACAATGCTGGCTATCCGGGTGCTAGCTGACCAGAACGT
A_04_P070742	TCTATTTACAGAACTGGATGCCAAGACTGTGACGGCAGAGGTACAGCCCCAGTGCGGCA
A_04_P003811	CCGCTGGTGACGCTGTTCCGCAACGCCATCGTCAAGAACCGGCACAAGAAGGGCCCCGTA
A_04_P034932	TTAAGATCCTCTCTGGGGTCATCCTGGAGGTGATCGCCGAGGAGTTTGCCAACGACTTCC
A_04_P002327	GGGGCCAGTTGTGGGGTCTTAATGCTCTTATTCTATCATGATTCCAGTTTGAGAAAAA
A_04_P089645	TGTGGGAGAAACTCAAGAACGAGAGAGAGTTTTAGTACACTTCTCCAATAGATATTTTA
A_04_P017086	TTGAGAGGAAGCTGCGGATAAAATCCAGCTTCGTGGCACCCTGGAGAAGGGCGTATGGGA
A_04_P089643	TTATTGTAATCCAGACACCATTGCTTCAACAAGATGGAGTCCATTGCCTTACCTGTGCTAT
A_04_P093249	ACTTATTACCTGAAGCTCGAGAACCAAGTCTGAAGAGCGTGAAGGTTGGAAGCATCAAG
A_04_P051682	AGATGATCCCAATCTGGTGAATGAGCCCTCTACAGATGAAACAGTTCTGGCTGATATCGA
A_04_P089644	CACTTCTCCAATAGATATTTTATTGTAATCCAGACACCATTGCTTCAACAAGATGGAGTC
A_04_P089642	TTGCTTCAAGATGGAGTCCATTGCCTTACCTGTGCTATGATGCTTCTCAATACGGATC
A_04_P089646	TTTTTAAAGGCTTTTCTCTTTGTGGGAGAACTCAAGAACGAGAGAGAGTTTTAGTACAC
A_04_P072427	TTCCTAGAAGGGAAACTGTTGAGAGAAAATCATGAATCAGAAGAAAAGACTCCAAAGGTG
A_04_P093247	TTATTACCTGAAGCTCGAGAACCAAGTCTGAAGAGCGTGAAGGTTGGAAGCATCAAGAC
A_04_P093248	CCTATTACCTGAAGCTCGAGAACCAAGTCTGAAGAGCGTGAAGGTTGGAAGCATCAAGA
A_04_P004291	ATATGGATAACAAGGGAAGCAGCTTTCATCGGGTCATCAAGGATTTTCATGATCCAAGGAGG
A_04_P093251	TTCTTCAAGGGCACTTATTACCTGAAGCTCGAGAACCAAGTCTGAAGAGCGTGAAGGTT
A_04_P001576	AACAACATCCTGGTGTAGTGCAAGATCCAGGAGCTCAAAAACGTGGCTTTGTTTGAAGAG
A_04_P088597	TTCCAAACAGAAGAAGAAGCTGGTAGGATCTCACAGGCTTTCCATTTATGAGGAGTGGGA
A_04_P001881	AAGGACAAGAAGCCATATTGCCGAAAGGATTTCTTAGCCATGTTCTACCCAAGTGTGGT
A_04_P097699	TTTTAAAGGATGGTCTTTCAGCCACTTGATCCAGATGGCCGAGTAAAAATGTGGGTTTA
A_04_P072428	ATTGAGCATGTGCAAAACTTTTATGATGGATTCTAGAAGGGAAACTGTTGAGAGAAAAT
A_04_P072431	TTCAAACGAAGAAGTCTCAGTACCAGCTTGACGATTTATCGAACTCTAGATGATGAG
A_04_P035132	ACAAGGAGAAGTTGAGACGGATGCACAGGCCTCTGGAGAGACTCCATCATCTCCCGC

Contd...

Supplementary Table 1: Contd....

Probe name	Sequence
A_04_P006131	ACTGCTGGTGAACCTGGAAGAGACGGAAACCCTGGATCAGATGGTCAGCCAGGCAGAGAT
A_04_P045978	TTGTTCTTCAAGACTGGTTCTTGCAGGATGCTTCATAAAACTCTGTCCACTTGTGCCTCC
A_04_P072429	TGGGATGCACTGCCATTACAGAAGTTTCAATTGAGCATGTGCAAAACTTTTATGATGGA
A_04_P056432	CTGGGAACAAGGAACAGGGTTACATGAGCCTCAAGGAGAACCAGATCTGTGTGGGCGTGG
A_04_P102148	TTGTTCTTCAAGACTGGTTCTTGCAGGATGCTTCATAAAACTCTGTCCACTTGTGCCTCC
A_04_P082384	GGACTGCAAGCCTTATAATAGAAGAAGATGACCCACTGAGGGATGGCTTCTTCTCAAGT
A_04_P033409	TGCCTTTTGTAGTGCATAAAAAGTACGTGTCCAGTGAAGCTGAAGACTTTTAAAGAAGA
A_04_P038492	CACAGTAAAAATGATCAGCTCGCCAGTGGGTGTGATTCTGACATCTACCACAAAAGAAGT
A_04_P058592	ACTTCTACGACTTCAAGTGGTCAACATCCGGGGCAAGCTGGTGTCTGCTGGAGAAGTACC
A_04_P059827	ATCTACGTCAACGACCACGAGGACAAGAACGAGGAGGCCTTCTGCGTGAAGGTCACCTAC
A_04_P095797	TCAAACCTCAAATTAAGGGCATGCCTCTGCTCCATACTTCGGGAAGCAAGAACCTTCAGT
A_04_P095799	GTTCAAACCTCAAATTAAGGGCATGCCTCTGCTCCATACTTCGGGAAGCAAGAACCTTCA
A_04_P099602	TATGATATTGGTGGTCTGATCAAGAATTTGGTGCAGGACGTTGGCCCTGTTTGTCTTTTA
A_04_P099603	ACGCAAGGCTGTGAGACTACCCATTATAGATATTGCACCCTATGATATTGGTGGTCTGA
A_04_P092587	CTTGTGATATTGCCTCTGGCAACCTGATGCATGCTACAAACCTATTGGAAAGCCTTAA
A_04_P054449	CGGGCAAATCCCTACTACTCAGAAGTTGAGCTCAATTCATCTCTGTTTTCTGGCCACAT
A_04_P083948	TACACTGTGTTACTCCACTCCTTAATCCTGTTGTGTACTCTTTGAGGAATAAGGAGGTC
A_04_P099605	ACAGCAAATTCACATACACAGTTCTGGAGGATGGCTGCTTAAACATACTGGGGAATGGA
A_04_P033287	TCTTTACAAGAGGAAACTGCAAGAAGGGGCCAGCTGGAGATAGAGGACCACGTGGAGAA
A_04_P029302	GCACATTTATATGTGTTCTTTTGTCTAATCTTGTCAACCAGTACAAGTGACCAACTA
A_04_P061512	AAGATGGTGAATGCTGGAACATCTTCACTTGAACAATTATATCAAACCTAGAG
A_04_P003721	TGCAAGAACAGCGTAGCCTACATGGACCAACAGACCGGCAACCTCAAGAAGTCCCTGCTC
A_04_P013577	GTACCATGAAATTGGAAGATCAATAGCAACTCTCATGACAGATGAGATTTTTCATGATGT
A_04_P053222	GAGGTAAAGCCTTATCTACTTGTGCATCCACTTTCTCTCCGTGTCTATATTCTATGGTT
A_04_P004432	GAGAATCAGCTGATGGACAACCGCTTCCAACCTGTAAACGCTGTCTACAGTCCCGACTTT
A_04_P099604	ACATACTGGGGAATGGAGCAAAACAGTCTTTGAATATAGAACACGCAAGGCTGTGAGACT
A_04_P097917	ATGAATATTCTCATCCGGGAAATCCGCCTATCGCTTCAACAATTAGACCTGGGGTTGAAG
A_04_P067988	TGTCGTTACGGTAGCTCAGATTGTCAAAAATGAAATGGAAAATGCCATAAAACTTTCTGT
A_04_P080226	CTACAGGTTGCAAAACATATTTCTTTGGTGTGTGTATCCTGTACTGATTTCCAATAG
A_04_P005106	ATACAAAACAATAAGCCATCTCGTTTGCCTTCTTGTATTTGATATTGCACCTTGGACATCGG
A_04_P080223	CAGGTTGCAAAACATATTTCTTTGGTGTGTGTATCCTGTACTGATTCCAATAGTTT
A_04_P075839	TCTACTGTACGTGACCAAAAGTCCTTAAAGGAAAAGAAGCTAAGCCTTCCAATGCCATCT
A_04_P080225	TACAGGTTGCAAAACATATTTCTTTGGTGTGTGTATCCTGTTACTGATTCCAATAGT
A_04_P002113	GGACAAGGCGACCGACTGAGCTCAGCTGCTTATTTATTGAAAATAAACAACACAAGAGTC
A_04_P075838	CTACTGTACGTGACCAAAAGTCCTTAAAGGAAAAGAAGCTAAGCCTTCCAATGCCATCTG
A_04_P083155	CAAAACCTATTGAAGTGTGTATGTACAGAGAACCATCACTACATGAAATTGGGGAAAAAC
A_04_P095802	ATTGTCAGTTTCTTAGCAAGGTTGGGCTGTTTCATCATGTCTGGACTATTTACGACCCAG
A_04_P029967	GTGGACGTTGGCCAGTCTGTTTCAAATAAGTGAACCTCCACTAAATTAATAAGAAAAGA
A_04_P051867	TGTGATCTTTGGCTGTGAGGTGTTTCGCTACCCCATGGCCTCCATCGAGTGGAGAAAGGA
A_04_P005011	AGAACTACAACATGTACATCTTCCCGTGCCTGGCAATTCGGCCAGCTGGACCAGCACC
A_04_P007976	TTGCTTCTCCAAGTACAAGTACTAGGTTGGCCATTATAATATCTATTTGGTGTAGTAA
A_04_P080222	GGTTCGAAACATATTTCTTTGGTGTGTGTATCCTGTTACTGATTCCAATAGTTTTG
A_04_P005107	TGGGGAAAAGACAATCATTGAATACAAAACAATAAGCCATCTCGTTTGCCTTCTTGTAT
A_04_P092167	TCAGATGACAAATATATGAAACACTGCAGGGTCAGGTTTCAACAGCTCTAGGGGAAGCA
A_04_P016398	GTTTGCCAAATTCGGAACCTGAAAGGTTTGTCTGTCTCTGGATGAATCAAATTTCTTCC
A_04_P083153	ATGAAATTGGGGAAAAACAAGGGCGTTTCAGGAAAAGCTCTGGAACACCAACTATGAATG
A_04_P005109	GCAGGTTCACTTACACTGTTCTTGTGATGGCTGCACGAAAAAGACAAATGAATGGGGAA
A_04_P033295	CCAAGGATGCACTATGGATGCTATCAAAGTTTACTGTGATTTCTCTACTGGCGAAACCTG
A_04_P033296	ACCAAGGATGCACTATGGATGCTATCAAAGTTTACTGTGATTTCTCTACTGGCGAAACCT
A_04_P033663	GCCCTACATCTTCAGACACAAATGATCAGGATATGATCTTCTCTGTTTTACACTGTCA
A_04_P033294	CAAGGATGCACTATGGATGCTATCAAAGTTTACTGTGATTTCTCTACTGGCGAAACCTGC
A_04_P033293	AAGATGCACTATGGATGCTATCAAAGTTTACTGTGATTTCTCTACTGGCGAAACCTGCA
A_04_P083152	GAGGAAAAGCTCTGGAACACCAACTATGAATGGAGGCAAGTCTGTAATCAAGACTCAAC
A_04_P034532	ATGAAGGTGGCAATGAGGAGAATATCAGCCAGCTGCTGTGTTCCAGAAGTTGTTTTAA
A_04_P033292	AGGATGCACTATGGATGCTATCAAAGTTTACTGTGATTTCTCTACTGGCGAAACCTGCAT
A_04_P041922	TACATACGCTTCCAAACTCTGAACCTGACAATCATTATGACTTTTGCCTCATACCGTGA

Contd...

Supplementary Table 1: Contd....

Probe name	Sequence
A_04_P041923	TTACATACGCTTCCAAACTCCTGAACCTGACAATCATTATGACTTTTGCCTCATACCGTG
A_04_P083154	TGTACAGAGAACCATCACTACATGAAATTGGGGAAAAACAAGGGCGTTTCGAGGAAAAAGCT
A_04_P100467	AAACATTACCAGCTGGATTTAGGCTAACCCACAACATCTGGGCAGTCACGGAAAATGACAG
A_04_P028651	TGCAATTTTGGTCTCCGCCACATAACCATTCTGAAGCTTTTGGGTGTTGGAGAGGAAGTT
A_04_P005108	CTTGTTCGATGGCTGCACGAAAAAGACAAATGAATGGGGAAAGACAATCATTGAATACAAA
A_04_P036902	TAATTCAGAGGGCGTCAAGATGGCTCCGTGGACTTTGACCGGCCCTGGGAAGCTTACAAGG
A_04_P082732	AGTGGTGAATATCAGTAGTTTGACAGGGTTTACAGGCTCTTGAAAACCTGCACGCGAAGACCT
A_04_P080444	ACTGATTGATGGCGAGTATAAGGATTACCTGGCATCTCATCCATTTCGACACAGAGACAAC
A_04_P080443	CTGATTGATGGCGAGTATAAGGATTACCTGGCATCTCATCCATTTCGACACAGAGACAAC
A_04_P089937	ACAAGCTGGACGTGGACATTTTGGCACAACCTGAAATACACTGGGTGTGTCATTAAGGAGA
A_04_P000416	TAGAAGAAAACCCCGTCGTGAAGACCCTCCTGGACGTCAACTGCCTGCTGTGCATCTGCT
A_04_P080445	AACTGATTGATGGCGAGTATAAGGATTACCTGGCATCTCATCCATTTCGACACAGAGACAA
A_04_P089787	CAACAACAACCTCCAAAAGAAGAGAATTGGAACCTACACAAACATGAACAAGTAGAAAAACC
A_04_P069826	TGCTGAACCATGGTATAAAGAAACCCTTACCAAAGAGACTATTCTCTGCCATTTTATAA
A_04_P080446	AAACTGATTGATGGCGAGTATAAGGATTACCTGGCATCTCATCCATTTCGACACAGAGACA
A_04_P098652	TTGTCATCAATCCCAACTACGAGGTCTCCGAGTCCGATTACTCCAACAACATCATGAAGT
A_04_P057962	AGTATGTGGAGTGCCTAGAAAAGAAAGTAGAGACTTTCACGTCGGAGAACACGAGCTGT
A_04_P035452	CTGTATTTGTAATCCAGGTCAGTGGCTGGTGGACACCTCCATGATTTTATCCTCATGCT
A_04_P069053	TCCGTGCATAGTTCTGACGAGAACATACTGTGTCACATTTGTCTGAGAAAATTGTTTCA
A_04_P089791	CACCAGTAAATCAAAGACTGAGTTGGGTGTTTCAAGAGTTAAATCTTTTCTTCCTGTTC
A_04_P069822	GAACCATGGTATAAAGAAACCCTTACCAAAGAGACTATTCTCTGCCATTTTATAAGCTT
A_04_P082177	CTAACCGAAGCTGAGAGACAGTTAATCCATGACTTTTATCACTTGGACTATTGATGTTT
A_04_P071528	GAAAATGTGAAGACTAAAGAAAAAACCTGGCACTTCGCTAGAGAGAACACCTGTTCCCA
A_04_P014266	GGCCTCGGACGAGGCCATTGAGAAGCTGTCCACGCTGTACTGGTTTACCCTAGAAATTTGG
A_04_P051042	ATGCTGGTTCGTGTACATTCGCTACCAGGACCAGACGGACGACGACGACGACGACGAGTGA
A_04_P002301	AAGCTTTTCGAGAAAGGATACAGCTGGAGTCAGTTTAGTGATGTGGAAGAGAACAGGACT
A_04_P027306	ATCATGTTTCGCCTTCTTCCCTGACAACCTTCAAGGCTGAAGTGAATAATGGTCTTTGAGCTG
A_04_P068184	CAAAAATCAATGAAATTCGCCAGATGTCTGGAGCTCAGATCAAAAATTGCCAACGCCACTG
A_04_P068182	AATCAATGAAATTCGCCAGATGTCTGGAGCTCAGATCAAAAATTGCCAACGCCACTGAAGG
A_04_P068183	AAATCAATGAAATTCGCCAGATGTCTGGAGCTCAGATCAAAAATTGCCAACGCCACTGAAG
A_04_P040043	GCCAGGGATAAAAAGTATCAATGCCTTGAATTTGGCTTCAAGGAAACTAAAGAGAAACCAA
A_04_P027309	TACATCAIGTTCGCCTTCTTCCCTGACAACCTTCAAGGCTGAAGTGAATAATGGTCTTTGAG
A_04_P068186	GACAAAAATCAATGAAATTCGCCAGATGTCTGGAGCTCAGATCAAAAATTGCCAACGCCAC
A_04_P012977	GTGCCTGGAACGGGAGTGACAGTGTGCATCATGACCGGGGCTTACAACAACCTTCTCCGCA
A_04_P068185	ACAAAAATCAATGAAATTCGCCAGATGTCTGGAGCTCAGATCAAAAATTGCCAACGCCACT
A_04_P003912	TTTATCTTCACCTTCTTCAAAGTTTCTGAGACCCGAGGCAGGACTTTTGAGGATATCACA
A_04_P027307	CATCATGTTTCGCCTTCTTCCCTGACAACCTTCAAGGCTGAAGTGAATAATGGTCTTTGAGCT
A_04_P074137	GAAAATGAAGATGACAACGTTGTCTTAGCATTTGAACAACCTGAGCGAAACCTTTTGTGAA
A_04_P074138	GGAGCAGCTTATATATTATTGAAAGATTTGCACTCACCATTAAGCTATCAGTGTTTCC
A_04_P057689	ACAAACTTTCAGGAACACAACCTTTCAGGCAGAAATCTCCAGCAGGTAATCTTGGGTA
A_04_P040042	TTAGACCTGGAAAGCTTGAGCCTCACGAGATTGGGCAAGCTGAAAGGAGAATTCAATGAA
A_04_P003626	GTTGAGCAGCTGTTTCGTTCTTGGTGGACAACCCTACACCAACTCCTACTCCTACTCGTG
A_04_P027308	ACATCATGTTTCGCCTTCTTCCCTGACAACCTTCAAGGCTGAAGTGAATAATGGTCTTTGAGC
A_04_P027310	CTACATCATGTTTCGCCTTCTTCCCTGACAACCTTCAAGGCTGAAGTGAATAATGGTCTTTGA
A_04_P082358	AAATGAGAAGATTTTCAGATGTGTCAGAACGTTTATTGGCTGTAAGGAACAAGGACAGAT
A_04_P003914	TCTTTATCTTCACCTTCTTCAAAGTTTCTGAGACCCGAGGCAGGACTTTTGAGGATATCA
A_04_P048467	ATTGTTTTTGAACCTGGTGTACCTTTAATTACACCTTAGCAGATGGAACCTGAAGTCAGT
A_04_P098422	AAAGGATGATGACATCAGCAGACTCTTGAATCGCTACCCAACCTGGATTAACATGGCCCA
A_04_P101047	TTAACATGGATGGTACAGCCCTTTATGAAGCGGTAGCTGCCATCTTTATAGCCCAAATGA
A_04_P003913	CTTTATCTTCACCTTCTTCAAAGTTTCTGAGACCCGAGGCAGGACTTTTGAGGATATCAC
A_04_P050054	TAACCTGAAGCTGTAATGAACCCAAGAAGAAGAAATATGCAAAAAGAGGCTTGGCCGGG
A_04_P050055	ATAACCTGAAGCTGTAATGAACCCAAGAAGAAGAAATATGCAAAAAGAGGCTTGGCCGG
A_04_P002261	TGACCCTTGACCTTTATCCTGAACCAACAGCATATGCATGCCAGGCTGGGCACGAGGCTCA
A_04_P050056	TATAACCCTGAAGCTGTAATGAACCCAAGAAGAAGAAATATGCAAAAAGAGGCTTGGCCG
A_04_P077452	GGACTGCCTTTACCCACCAGACTAAAAGATTACTTGGAAGAATATAAATTCAGGTATAA
A_04_P077456	CTGGGGACTGCCTTTACCCACCAGACTAAAAGATTACTTGGAAGAATATAAATTCAGGT

Contd...

Supplementary Table 1: Contd....

Probe name	Sequence
A_04_P077453	GGGACTGCCTTTACCCACCAGACTAAAAGATTACTTGGGAAGAATATAAATTCAGGTATA
A_04_P002438	TACTGAGAAACCAGGAACCGAAGAATCAATTGTAAGTGAAGAGTTAATTGTAGTTACTTC
A_04_P003915	TTCTTTATCTTCACCTTCTTCAAAGTTCCTGAGACCCGAGGCAGGACTTTTGAGGATATC
A_04_P002437	GTATACTTTAGGACAATGCAGACAGTCTGAAAAAGAGAAAATGGAGCAAAAAGGCCATTTTC
A_04_P001796	ACTTACTATGACCAGGAGCGGAAGATGAACATGAAGGACAACGTCAGGCCGCTGCAGCG
A_04_P000366	GCACAGTTACCCAAGATATTGGCAGGGATGGTGAACCACCTTCTCTTTCATAAAAAAGTGA
A_04_P092835	GACTAAGCGACACCAGAAAATTCACCCATTTTTTACCCAGGCCAGTAGATCCTTCTAAGTT
A_04_P092832	TAAGCGACACCAGAAAATTCACCCATTTTTTACCCAGGCCAGTAGATCCTTCTAAGTTGCC
A_04_P092834	ACTAAGCGACACCAGAAAATTCACCCATTTTTTACCCAGGCCAGTAGATCCTTCTAAGTTG
A_04_P084832	CAAGTCTTGCTTAGAAAAATCAAGAGAAGCAGAATCCATGGCAACTCACCACCTTCCATGA
A_04_P092833	CTAAGCGACACCAGAAAATTCACCCATTTTTTACCCAGGCCAGTAGATCCTTCTAAGTTGC
A_04_P000367	TTTATCCAGTCCCGGGCGCTGAGTGTGAATTTCCAGAAAATGATGTCTGAAGTTATTGCT
A_04_P095007	AAGGTTAATTTAGCCAACGAGCCAAAGTACCGCCTGGACACAGTGA AAAATGAGGTCTAA
A_04_P059047	TCTACTTCAACGTGGGCAAGCTGAAGCAGGAGATGGGTGGCATCGTGACCGAGATCATCC
A_04_P014040	GCAGGAAAAGTACAAAAGCCAGATTTTGCATTTTGAAGAAGCCAAGGCCACCATCCATGA
A_04_P068197	AAAGGCAAGAGGTTACGTACAAGTTCAACTTCAGCAAGCTCATCGTGGTCAACTATCCT
A_04_P084833	TTCAACCCCTCAGCAGAATATTCACTGGCTGAACTTGATGAGAAAATTAGTGCCCTCA
A_04_P084834	TGGAAGGCATCTCTCCTGAATACTTTCAGTCTATAAACTTTTCTGGAAAAAGAAGAAAAG
A_04_P014038	AGGAAAAGTACAAAAGCCAGATTTTGCATTTTGAAGAAGCCAAGGCCACCATCCATGAGA
A_04_P071088	AGTTTCAAAGAGAACCTGAAGTGCTTCTGTGTTGTCATCCCTTTAACTGCTGGGAGCCA
A_04_P003501	TATCAACAGTGATGGGGCCATCAACTTCCAGGAGTTCCTCATACTGATTGTGAAGATAGG
A_04_P035696	GTATGCCAAGAGGGCATTCTGCACCTGGTACATTCAAGAAAGGCATGGAACAAGGAGAATT
A_04_P013130	TCAGTACTCGAAGAAAAAGGATGCAGACTCTTGGTTCAAAGAGCTGGATATCAACAGTGA
A_04_P013126	TACTCGAAGAAAAAGGATGCAGACTCTTGGTTCAAAGAGCTGGATATCAACAGTGACGGG
A_04_P003502	ATATCAACAGTGATGGGGCCATCAACTTCCAGGAGTTCCTCATACTGATTGTGAAGATAG
A_04_P060934	TTGCTAAAAGTCTGACCCCTAATAACACCATTAGAGAATGGCAAATGTTTTCTGTATCG
A_04_P003503	GATATCAACAGTGATGGGGCCATCAACTTCCAGGAGTTCCTCATACTGATTGTGAAGATA
A_04_P003505	TGGATATCAACAGTGATGGGGCCATCAACTTCCAGGAGTTCCTCATACTGATTGTGAAGA
A_04_P003504	GGATATCAACAGTGATGGGGCCATCAACTTCCAGGAGTTCCTCATACTGATTGTGAAGAT

POMC: Proopiomelanocortin, GalNAc-T6: UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 6; FAM46A: Family with sequence similarity 46, member A; *C. elegans*: *Caenorhabditis elegans*; CRP: C-reactive protein; SLC17A5: Solute carrier family 17 (acidic sugar transporter), member 5; MRP-8: Macrophage migration inhibitory factor-related protein-8; KCNE2: Potassium voltage-gated channel, Isk-related family, member 2; PGR: Progesterone receptor; CA4: Carbonic anhydrase 4; STK17A: Serine/threonine kinase 17A; SOC2: Suppressor of cytokine signaling 2; PRKCZ: Protein kinase C, zeta; IFIT1B: Interferon-induced protein with tetratricopeptide repeats 1B; TE: TMEM30B: Transmembrane protein 30B; CTTNBP2: Cortactin binding protein 2; PTPRF: Protein tyrosine phosphatase, receptor type, f polypeptide; PPFIA2: Protein tyrosine phosphatase, receptor type, f polypeptide alpha 2; COL1A2: Collagen, Type I, alpha 2; BCL2L1: BCL2-like 1; SLC4A7: Solute carrier family 4, sodium bicarbonate cotransporter, member 7; GPX7: Glutathione peroxidase 7; LPXN: Leupaxin; PRLR: Prolactin receptor; *O. cuniculus*: *Oryctolagus cuniculus*; CSF: Colony stimulating factor; MMP: Matrix metalloproteinase.

Supplementary Table 2: Differentially expressed genes

Probe name	P (drug)	FC ([M-T] vs. [M-C])	Log FC ([M-T] vs. [M-C])	FC (abs) ([M-T] vs. [M-C])	Regulation ([M-T] vs. [M-C])	Gene symbol	Description
A_04_P090206	0.002592394	-34.987576	-5.128771	34.987576	Down	BRINP3	Bone morphogenetic protein/retinoic acid inducible neural-specific 3 (source: HGNC symbol; Acc.: 22393) (ENSOCUT00000011729)
A_04_P087007	8.36E-04	5.183949	2.3740516	5.183949	Up	NIM1K	NIM1 serine/threonine protein kinase (source: HGNC symbol; Acc.: 28646) (ENSOCUT00000017806)
A_04_P090204	0.013964647	-35.64766	-5.1557355	35.64766	Down	BRINP3	Bone morphogenetic protein/retinoic acid inducible neural-specific 3 (source: HGNC symbol; Acc.: 22393) (ENSOCUT00000011729)
A_04_P087010	0.001353522	5.4337707	2.4419537	5.4337707	Up	NIM1K	NIM1 serine/threonine protein kinase (source: HGNC symbol; Acc.: 28646) (ENSOCUT00000017806)
A_04_P087008	0.001162031	5.077875	2.344225	5.077875	Up	NIM1K	NIM1 serine/threonine protein kinase (source: HGNC symbol; Acc.: 28646) (ENSOCUT00000017806)
A_04_P087009	6.51E-04	6.1899066	2.6299176	6.1899066	Up	NIM1K	NIM1 serine/threonine protein kinase (source: HGNC symbol; Acc.: 28646) (ENSOCUT00000017806)
A_04_P090205	0.010273683	-32.678364	-5.030264	32.678364	Down	BRINP3	Bone morphogenetic protein/retinoic acid inducible neural-specific 3 (source: HGNC symbol; Acc.: 22393) (ENSOCUT00000011729)
A_04_P087011	0.001393298	5.334261	2.4152884	5.334261	Up	NIM1K	NIM1 serine/threonine protein kinase (source: HGNC symbol; Acc.: 28646) (ENSOCUT00000017806)
A_04_P089349	1.41E-04	-2.0694027	-1.0492144	2.0694027	Down	CHRNA2	Cholinergic receptor, nicotinic, alpha 2 (neuronal) (source: HGNC symbol; Acc.: 1956) (ENSOCUT00000007679)
A_04_P000511	0.014765256	18.562225	4.214298	18.562225	Up	RFT-II	<i>O. cuniculus</i> galactoside 2-L-fucosyltransferase (RFT-II), mRNA (NM_001082402)
A_04_P095722	0.014857199	-3.2431571	-1.6973989	3.2431571	Down	MOB3B	MOB kinase activator 3B (source: HGNC symbol; Acc.: 23825) (ENSOCUT00000017680)
A_04_P000512	0.029247807	11.233361	3.4897177	11.233361	Up	RFT-II	<i>O. cuniculus</i> galactoside 2-L-fucosyltransferase (RFT-II), mRNA (NM_001082402)
A_04_P061367	6.82E-04	2.03939	-1.0281377	2.03939	Down	TPK1	Thiamin pyrophosphokinase 1 (source: HGNC symbol; Acc.: 17358) (ENSOCUT00000003405)
A_04_P044995	1.77E-04	-2.0282369	-1.0202261	2.0282369	Down	LOC100346337	Uncharacterized protein (source: UniProtKB/TrEMBL; Acc.: G1U4C5) (ENSOCUT00000026037)
A_04_P039523	4.39E-05	-2.037557	-1.0268403	2.037557	Down	LOC100346673	Uncharacterized protein (source: UniProtKB/TrEMBL; Acc.: G1TUR2) (ENSOCUT00000024312)
A_04_P095726	0.002862763	-3.7613301	-1.911243	3.7613301	Down	MOB3B	MOB kinase activator 3B (source: HGNC symbol; Acc.: 23825) (ENSOCUT00000017680)
A_04_P000514	0.044802833	9.408754	3.2340038	9.408754	Up	RFT-II	<i>O. cuniculus</i> galactoside 2-L-fucosyltransferase (RFT-II), mRNA (NM_001082402)
A_04_P003594	0.003417118	-2.465992	-1.3021681	2.465992	Down	LOC100009480	<i>O. cuniculus</i> lipophilin CS (LOC100009480), mRNA (NM_001082723)
A_04_P081503	0.022404155	-17.285624	-4.1115007	17.285624	Down	GRIA2	Glutamate receptor, ionotropic, AMPA 2 (source: HGNC symbol; Acc.: 4572) (ENSOCUT00000026179)

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Supplementary Table 2: Contd...

Probe name	P (drug)	FC ([M-T] vs. [M-C])	Log FC ([M-T] vs. [M-C])	FC (abs) ([M-T] vs. [M-C])	Regulation ([M-T] vs. [M-C])	Gene symbol	Description
A_04_P002146	0.016625658	3.2863083	1.7164679	3.2863083	Up	NOS3	<i>O. cuniculus</i> nitric oxide synthase 3 (endothelial cell) (NOS3), mRNA (NM_001082733)
A_04_P095723	0.011801046	-2.7260911	-1.4468338	2.7260911	Down	MOB3B	MOB kinase activator 3B (source: HGNC symbol; Acc.: 23825) (ENSOCUT00000017680)
A_04_P095724	0.037129164	-2.9672625	-1.5691326	2.9672625	Down	MOB3B	MOB kinase activator 3B (source: HGNC symbol; Acc.: 23825) (ENSOCUT00000017680)
A_04_P061519	3.86E-04	-2.0915723	-1.0645878	2.0915723	Down	TMPRSS12	Transmembrane (C-terminal) protease, serine 12 (source: HGNC symbol; Acc.: 28779) (ENSOCUT00000012143)
A_04_P000515	0.028941542	11.739163	3.5532577	11.739163	Up	RFT-II	<i>O. cuniculus</i> galactoside 2-L-fucosyltransferase (RFT-II), mRNA (NM_001082402)
A_04_P008321	0.004462368	2.1547623	1.1075287	2.1547623	Up	CTSF	Cathepsin F (source: HGNC symbol; Acc.: 2531) (ENSOCUT00000013703)
A_04_P027308	0.015789868	-8.41193	-3.0724368	8.41193	Down	VIPR1	Uncharacterized protein (source: UniProtKB/TrEMBL; Acc.: G1T4R1) (ENSOCUT00000013108)
A_04_P089820	0.008767877	2.8675928	1.5198402	2.8675928	Up	TMEM81	Transmembrane protein 81 (source: HGNC symbol; Acc.: 32349) (ENSOCUT00000015420)
A_04_P019731	0.014666528	2.1310256	1.091548	2.1310256	Up	DST	Predicted: <i>O. cuniculus</i> dystonin (LOC100345428), miscRNA (XR_085126)
A_04_P051957	5.14E-05	-2.0692248	-1.0490904	2.0692248	Down	SSTR2	Somatostatin receptor 2 (source: HGNC symbol; Acc.: 11331) (ENSOCUT00000009346)
A_04_P077947	1.37E-04	-2.1267912	-1.0886784	2.1267912	Down	PLEKHG6	Pleckstrin homology domain containing, family G (with Rho GEF domain) member 6 (source: HGNC symbol; Acc.: 25562) (ENSOCUT00000010134)
A_04_P027310	0.016151104	-7.2762876	-2.8632026	7.2762876	Down	VIPR1	Uncharacterized protein (source: UniProtKB/TrEMBL; Acc.: G1T4R1) (ENSOCUT00000013108)
A_04_P099127	0.03358519	2.1944575	1.1338644	2.1944575	Up	DST	Predicted: <i>O. cuniculus</i> dystonin (LOC100345428), miscRNA (XR_085126)
A_04_P033412	0.036582667	3.468556	1.7943351	3.468556	Up	CCNE1	Cyclin E1 (source: HGNC symbol; Acc.: 1589) (ENSOCUT00000009147)
A_04_P067484	0.031035315	-2.4192803	-1.2745779	2.4192803	Down	GPRC5D	G protein-coupled receptor, family C, group 5, member D (source: HGNC symbol; Acc.: 13310) (ENSOCUT00000015334)
A_04_P095725	0.013923194	-2.5073705	-1.3261752	2.5073705	Down	MOB3B	MOB kinase activator 3B (source: HGNC symbol; Acc.: 23825) (ENSOCUT00000017680)
A_04_P072427	0.002985839	9.581865	3.2603066	9.581865	Up	ERP27	Endoplasmic reticulum protein 27 (source: HGNC symbol; Acc: 26495) (ENSOCUT00000006001)
A_04_P080361	0.006089133	-3.159741	-1.6598063	3.159741	Down	LOC100346813	
A_04_P087084	0.016522828	2.0852642	1.0602303	2.0852642	Up	HECTD2	HECT domain containing E3 ubiquitin protein ligase 2 (source: HGNC symbol; Acc.: 26736) (ENSOCUT00000015038)

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Supplementary Table 2: Contd...

Probe name	P (drug)	FC ([M-T] vs. [M-C])	Log FC ([M-T] vs. [M-C])	FC (abs) ([M-T] vs. [M-C])	Regulation ([M-T] vs. [M-C])	Gene symbol	Description
A_04_P050163	0.024847375	4.961795	2.310862	4.961795	Up	OTC	Ornithine carbamoyltransferase (source: HGNC symbol; Acc.: 8512) (ENSOCUT00000025516)
A_04_P004291	0.00428289	2.3938737	1.259347	2.3938737	Up	PPIC	Peptidylprolyl isomerase C (cyclophilin C) (source: HGNC symbol; Acc.: 9256) (ENSOCUT00000012051)
A_04_P067977	0.023129197	-2.4537835	-1.295008	2.4537835	Down	KRT75	Keratin 75 (source: HGNC symbol; Acc.: 24431) (ENSOCUT00000002625)
A_04_P072197	4.02E-05	-2.014058	-1.0101054	2.014058	Down	SLC13A5	Solute carrier family 13 (sodium-dependent citrate transporter), member 5 (source: HGNC symbol; Acc.: 23089) (ENSOCUT00000009882)
A_04_P042687	0.018582681	-3.9991665	-1.9996994	3.9991665	Down	CCL24	Uncharacterized protein (source: UniProtKB/TrEMBL; Acc.: G1SCU3) (ENSOCUT00000000207)
A_04_P102467	0.040627208	17.093897	4.0954094	17.093897	Up	UPK1B	Uroplakin 1B (source: HGNC symbol; Acc.: 12578) (ENSOCUT00000008290)
A_04_P072430	0.007601973	4.6499896	2.2172275	4.6499896	Up	ERP27	Endoplasmic reticulum protein 27 (source: HGNC symbol; Acc.: 26495) (ENSOCUT00000006001)
A_04_P005044	0.008999595	2.1767006	1.1221429	2.1767006	Up	NRG1	Neuregulin 1 (source: HGNC symbol; Acc.: 7997) (ENSOCUT00000005836)
A_04_P073707	0.013036333	-2.2599533	-1.1762929	2.2599533	Down	ACE	<i>O. cuniculus</i> ACE, transcript variant 2, mRNA (NM_001171069)
A_04_P001576	0.023132525	2.3510208	1.2332873	2.3510208	Up	PRLR	<i>O. cuniculus</i> PRLR, mRNA (NM_001082231)
A_04_P002261	0.01926593	-3.3654182	-1.7507858	3.3654182	Down	PRKCZ	<i>O. cuniculus</i> PRKCZ, mRNA (NM_001082758)
A_04_P067467	0.0211376	3.9657516	1.9875944	3.9657516	Up	HDX	Highly divergent homeobox (source: HGNC symbol; Acc.: 26411) (ENSOCUT00000000902)
A_04_P050162	0.028948016	4.5407467	2.1829295	4.5407467	Up	OTC	Ornithine carbamoyltransferase (source: HGNC symbol; Acc.: 8512) (ENSOCUT00000025516)
A_04_P072428	0.00370054	6.5761867	2.7172513	6.5761867	Up	ERP27	Endoplasmic reticulum protein 27 (source: HGNC symbol; Acc.: 26495) (ENSOCUT00000006001)
A_04_P072431	0.007255266	5.6238146	2.491549	5.6238146	Up	ERP27	Endoplasmic reticulum protein 27 (source: HGNC symbol; Acc.: 26495) (ENSOCUT00000006001)
A_04_P068348	0.009709035	-2.018818	-1.0135107	2.018818	Down	TNFSF8	Tumor necrosis factor (ligand) superfamily, member 8 (source: HGNC symbol; Acc.: 11938) (ENSOCUT00000009975)
A_04_P013032	0.041744873	-3.750062	-1.9069145	3.750062	Down	LBP	<i>O. cuniculus</i> LBP, mRNA (NM_001195719)
A_04_P060608	0.01998477	3.5962288	1.8464848	3.5962288	Up	ALDH1L2	Aldehyde dehydrogenase 1 family, member L2 (source: HGNC symbol; Acc.: 26777) (ENSOCUT00000006965)
A_04_P088684	0.029921694	3.0602467	1.6136479	3.0602467	Up	NUF2	NUF2, NDC80 kinetochore complex component (source: HGNC symbol; Acc.: 14621) (ENSOCUT00000001171)
A_04_P096167	0.02870236	-2.2684171	-1.1816859	2.2684171	Down	TMEFF2	Transmembrane protein with EGF-like and two follistatin-like domains 2 (source: HGNC symbol; Acc.: 11867) (ENSOCUT00000001723)

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Supplementary Table 2: Contd...

Probe name	P (drug)	FC ([M-T] vs. [M-C])	Log FC ([M-T] vs. [M-C])	FC (abs) ([M-T] vs. [M-C])	Regulation ([M-T] vs. [M-C])	Gene symbol	Description
A_04_P046043	0.030908667	2.080366	1.0568373	2.080366	Up	OLFR651_1	<i>O. cuniculus</i> olfactory receptor 651 (OLFR651_1), mRNA (NM_001171473)
A_04_P072429	0.009909939	5.4365892	2.4427018	5.4365892	Up	ERP27	Endoplasmic reticulum protein 27 (source: HGNC symbol; Acc.: 26495) (ENSOCUT00000006001)
A_04_P088407	0.028551526	-2.1645124	-1.114042	2.1645124	Down	SLC7A8	<i>O. cuniculus</i> solute carrier family 7 (amino acid transporter light chain, L system), member 8 (SLC7A8), mRNA (NM_001082682)
A_04_P075700	0.034938697	-2.0471556	-1.0336208	2.0471556	Down	TYMS	Thymidylate synthetase (source: HGNC symbol; Acc.: 12441) (ENSOCUT00000008664)
A_04_P062848	2.81E-04	-2.7127166	-1.4397383	2.7127166	Down	CREM	cAMP responsive element modulator (source: HGNC symbol; Acc.: 2352) (ENSOCUT00000001657)
A_04_P069025	0.036677245	-2.6477945	-1.4047911	2.6477945	Down	FAM150A	Family with sequence similarity 150, member A (source: HGNC symbol; Acc.: 33775) (ENSOCUT00000033417)
A_04_P066317	0.025779523	2.3580089	1.2375691	2.3580089	Up	VASH1	Vasohibin 1 (source: HGNC symbol; Acc.: 19964) (ENSOCUT00000009526)
A_04_P012981	0.001837161	-2.371969	-1.2460852	2.371969	Down	TGFA	Transforming growth factor, alpha (source: HGNC symbol; Acc.: 11765) (ENSOCUT00000033653)
A_04_P062593	0.014280057	2.2826567	1.1907139	2.2826567	Up	LOC100353757	Uncharacterized protein (source: UniProtKB/TrEMBL; Acc.: G1SJJ6) (ENSOCUT00000003365)
A_04_P075697	0.032748736	-2.02286	-1.0163965	2.02286	Down	TYMS	Thymidylate synthetase (source: HGNC symbol; Acc.: 12441) (ENSOCUT00000008664)
A_04_P056382	0.03879594	-2.1264076	-1.0884182	2.1264076	Down	ITGAX	Integrin, alpha X (complement component 3 receptor 4 subunit) (source: HGNC symbol; Acc.: 6152) (ENSOCUT00000017426)
A_04_P075699	0.0334667	-2.014203	-1.0102091	2.014203	Down	TYMS	Thymidylate synthetase (source: HGNC symbol; Acc.: 12441) (ENSOCUT00000008664)
A_04_P075047	0.03242162	3.6401513	1.8639984	3.6401513	Up	B3GALNT1	Beta-1,3-N-acetylgalactosaminyltransferase 1 (globoside blood group) (source: HGNC symbol; Acc.: 918) (ENSOCUT00000001174)
A_04_P064848	0.006981436	-2.088532	-1.0624893	2.088532	Down	IL12B	Interleukin 12B (natural killer cell stimulatory factor 2, cytotoxic lymphocyte maturation factor 2, p40) (source: HGNC symbol; Acc.: 5970) (ENSOCUT00000016318)
A_04_P080600	0.039867163	3.140103	1.6508119	3.140103	Up	EYS	Predicted: <i>O. cuniculus</i> eyes shut homolog (<i>Drosophila</i>) (EYS), mRNA (XM_008263282)
A_04_P049942	0.016367858	8.123102	3.0220308	8.123102	Up	ADAD1	Adenosine deaminase domain containing 1 (testis-specific) (source: HGNC symbol; Acc.: 30713) (ENSOCUT00000012988)
A_04_P013965	4.85E-05	-2.376971	-1.2491243	2.376971	Down	HTR3B	5-hydroxytryptamine (serotonin) receptor 3B, ionotropic (source: HGNC symbol; Acc.: 5298) (ENSOCUT00000033424)

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Supplementary Table 2: Contd...

Probe name	P (drug)	FC ([M-T] vs. [M-C])	Log FC ([M-T] vs. [M-C])	FC (abs) ([M-T] vs. [M-C])	Regulation ([M-T] vs. [M-C])	Gene symbol	Description
A_04_P079624	0.047004465	2.2268746	1.1550202	2.2268746	Up	RIC8B	RIC8 GEFB (source: HGNC symbol; Acc.: 25555) (ENSOCUT00000006126)
A_04_P042877	0.013875492	-2.0739286	-1.0523663	2.0739286	Down	HIF3A	Predicted: <i>O. cuniculus</i> hypoxia inducible factor 3, alpha subunit (HIF3A), mRNA (XM_008252146)
A_04_P040417	0.028284287	-2.9792025	-1.5749261	2.9792025	Down	BPIFA3	BPI fold containing family A, member 3 (source: HGNC symbol; Acc.: 16204) (ENSOCUT00000015715)
A_04_P062478	0.014490645	2.4385202	1.286006	2.4385202	Up	LOC100349425	Predicted: <i>O. cuniculus</i> exocyst complex component 1-like (LOC100349425), mRNA (XM_002717166)
A_04_P054449	0.002579865	-2.1617088	-1.1121722	2.1617088	Down	MMP1	<i>O. cuniculus</i> matrix metalloproteinase 1 (interstitial collagenase) (MMP1), mRNA (NM_001171139)
A_04_P005094	0.009245173	-2.4121513	-1.2703204	2.4121513	Down	CER1	Cerberus 1, DAN family BMP antagonist (source: HGNC symbol; Acc.: 1862) (ENSOCUT00000010373)
A_04_P088683	0.019200655	3.6019692	1.8487859	3.6019692	Up	NUF2	NUF2, NDC80 kinetochore complex component (source: HGNC symbol; Acc.: 14621) (ENSOCUT00000001171)
A_04_P013087	0.008903244	-2.3892436	-1.2565539	2.3892436	Down	CYP19A1	CYP19A1, mRNA (source: RefSeq mRNA; Acc.: NM_001170921) (ENSOCUT00000012304)
A_04_P075049	0.037794687	3.6455815	1.866149	3.6455815	Up	B3GALNT1	Beta-1,3-N-acetylgalactosaminyltransferase 1 (globoside blood group) (source: HGNC symbol; Acc.: 918) (ENSOCUT00000001174)
A_04_P047767	0.04342047	2.0973828	1.0685902	2.0973828	Up	GCH1	GTP cyclohydrolase 1 (source: HGNC symbol; Acc.: 4193) (ENSOCUT00000003056)
A_04_P075048	0.029252984	4.014885	2.0053587	4.014885	Up	B3GALNT1	Beta-1,3-N-acetylgalactosaminyltransferase 1 (globoside blood group) (source: HGNC symbol; Acc.: 918) (ENSOCUT00000001174)
A_04_P087172	0.048340406	-2.159121	-1.1104441	2.159121	Down	ARHGEF38	Rho GEF 38 (source: HGNC symbol; Acc.: 25968) (ENSOCUT00000008875)
A_04_P069977	0.008163161	-2.248162	-1.168746	2.248162	Down	TREML1	Triggering receptor expressed on myeloid cells-like 1 (source: HGNC symbol; Acc.: 20434) (ENSOCUT00000007264)
A_04_P087082	0.02962216	2.0231328	1.0165911	2.0231328	Up	HECTD2	HECT domain containing E3 ubiquitin protein ligase 2 (source: HGNC symbol; Acc.: 26736) (ENSOCUT00000015038)
A_04_P086101	0.008958133	2.2865772	1.1931896	2.2865772	Up	SPATS1	Spermatogenesis associated, serine-rich 1 (source: HGNC symbol; Acc.: 22957) (ENSOCUT00000017228)
A_04_P101877	0.03837728	3.0359862	1.6021652	3.0359862	Up	ITGBL1	Integrin, beta-like 1 (with EGF-like repeat domains) (source: HGNC symbol; Acc.: 6164) (ENSOCUT00000008813)

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Supplementary Table 2: Contd...

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A_04_P098065	0.02010309	-2.2379515	-1.1621788	2.2379515	Down	LRRD1	Leucine-rich repeats and death domain containing 1 (source: HGNC symbol; Acc.: 34300) (ENSOCUT0000004562)
A_04_P020052	0.033614933	-3.511037	-1.8118973	3.511037	Down	LRRN1	Predicted: <i>O. cuniculus</i> leucine rich repeat protein 1, neuronal-like (LOC100344514), mRNA (XM_002720615)
A_04_P018421	0.008912688	2.1848788	1.1275532	2.1848788	Up	GNGT1	Guanine nucleotide binding protein (G protein), gamma transducing activity polypeptide 1 (source: HGNC symbol; Acc.: 4411) (ENSOCUT00000017033)
A_04_P057677	0.0182536	-2.1814566	-1.1252918	2.1814566	Down	SLC34A2	Solute carrier family 34 (Type II sodium/phosphate cotransporter), member 2 (source: HGNC symbol; Acc.: 11020) (ENSOCUT00000002945)
A_04_P101879	0.039996047	2.7649012	1.4672279	2.7649012	Up	ITGBL1	Integrin, beta-like 1 (with EGF-like repeat domains) (source: HGNC symbol; Acc.: 6164) (ENSOCUT00000008813)
A_04_P004576	0.036671165	14.257102	3.8336089	14.257102	Up	MYH1	<i>O. cuniculus</i> myosin, heavy chain 1, skeletal muscle, adult (MYH1), mRNA (NM_001109816)
A_04_P055525	0.001051425	-2.5741715	-1.3641082	2.5741715	Down	TMEM176B	Transmembrane protein 176B (source: HGNC symbol; Acc.: 29596) (ENSOCUT00000016892)
A_04_P005121	0.00654842	-2.6257641	-1.3927374	2.6257641	Down	HTR3B	5-hydroxytryptamine (serotonin) receptor 3B, ionotropic (source: HGNC symbol; Acc.: 5298) (ENSOCUT00000033424)
A_04_P070787	0.0238121	2.6723764	1.4181232	2.6723764	Up	DTL	Denticleless E3 ubiquitin protein ligase homolog (<i>Drosophila</i>) (source: HGNC symbol; Acc.: 30288) (ENSOCUT00000000436)
A_04_P003182	2.57E-04	3.0989883	1.6317973	3.0989883	Up	CGA	<i>O. cuniculus</i> glycoprotein hormones, alpha polypeptide (CGA), mRNA (NM_001082724)
A_04_P070344	0.021318257	3.801474	1.926559	3.801474	Up	LECT2	Leukocyte cell-derived chemotaxin 2 (source: HGNC symbol; Acc.: 6550) (ENSOCUT00000006379)
A_04_P047768	0.037755918	2.0804737	1.056912	2.0804737	Up	GCH1	GTP cyclohydrolase 1 (source: HGNC symbol; Acc.: 4193) (ENSOCUT00000003056)
A_04_P006369	0.009818262	-2.6181357	-1.3885399	2.6181357	Down	WIPI1	WD repeat domain, phosphoinositide interacting 1 (source: HGNC symbol; Acc.: 25471) (ENSOCUT00000017410)
A_04_P062481	0.038461924	2.4462638	1.29058	2.4462638	Up	LOC100349425	Predicted: <i>O. cuniculus</i> exocyst complex component 1-like (LOC100349425), mRNA (XM_002717166)
A_04_P047771	0.03879093	2.0867136	1.0612326	2.0867136	Up	GCH1	GTP cyclohydrolase 1 (source: HGNC symbol; Acc.: 4193) (ENSOCUT00000003056)
A_04_P013034	0.026828822	-3.5224009	-1.8165591	3.5224009	Down	LBP	<i>O. cuniculus</i> LBP, mRNA (NM_001195719)
A_04_P101515	0.009637895	2.476038	1.3080335	2.476038	Up	CTNNA2	Catenin (cadherin-associated protein), alpha 2 (source: HGNC symbol; Acc.: 2510) (ENSOCUT00000033690)

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A_04_P086097	0.02128666	3.6858408	1.8819938	3.6858408	Up	SPATS1	Spermatogenesis associated, serine-rich 1 (source: HGNC symbol; Acc.: 22957) (ENSOCUT00000017228)
A_04_P072187	0.027534235	2.45875	1.297925	2.45875	Up	GEM	GTP binding protein overexpressed in skeletal muscle (source: HGNC symbol; Acc.: 4234) (ENSOCUT0000001030)
A_04_P101880	0.042139802	2.7761517	1.4730864	2.7761517	Up	ITGBL1	Integrin, beta-like 1 (with EGF-like repeat domains) (source: HGNC symbol; Acc.: 6164) (ENSOCUT00000008813)
A_04_P012961	0.025834136	2.3093436	1.2074828	2.3093436	Up	ACE-1	<i>O. cuniculus</i> acetylcholinesterase mRNA, partial cds (U05036)
A_04_P062762	0.017634036	-2.2404964	-1.1638184	2.2404964	Down	EPHA8	EPH receptor A8 (source: HGNC symbol; Acc.: 3391) (ENSOCUT00000015118)
A_04_P004386	0.039384972	2.1704316	1.1179819	2.1704316	Up	TIMP4	<i>O. cuniculus</i> TIMP metalloproteinase inhibitor 4 (TIMP4), mRNA (NM_001195690)
A_04_P079312	0.028580146	5.5793986	2.4801097	5.5793986	Up	NR4A3	Nuclear receptor subfamily 4, group A, member 3 (source: HGNC symbol; Acc.: 7982) (ENSOCUT0000000737)
A_04_P047770	0.019225257	2.0568469	1.0404344	2.0568469	Up	GCH1	GTP cyclohydrolase 1 (source: HGNC symbol; Acc.: 4193) (ENSOCUT00000003056)
A_04_P072188	0.02921553	2.3160188	1.211647	2.3160188	Up	GEM	GTP binding protein overexpressed in skeletal muscle (source: HGNC symbol; Acc.: 4234) (ENSOCUT0000001030)
A_04_P034787	0.037558276	-2.7561917	-1.4626763	2.7561917	Down	LOC100351425	Uncharacterized protein (source: UniProtKB/TrEMBL; Acc.: G1T522) (ENSOCUT00000013261)
A_04_P084832	0.011172667	-2.3737729	-1.2471819	2.3737729	Down	MBIP	MAP3K12 binding inhibitory protein 1 (source: HGNC symbol; Acc.: 20427) (ENSOCUT00000017089)
A_04_P050376	0.001221032	-2.6195357	-1.3893111	2.6195357	Down	ODF4	Outer dense fiber of sperm tails 4 (source: HGNC symbol; Acc.: 19056) (ENSOCUT00000015082)
A_04_P016399	0.02350145	-2.692988	-1.4292078	2.692988	Down	FKBP1B	nbc39d02.x1 Rabbit trigeminal nerve. Unnormalized (nbc) <i>O. cuniculus</i> cDNA clone nbc39d02 3', mRNA sequence (EB378230)
A_04_P064617	0.001882354	-2.809861	-1.4904988	2.809861	Down	HUNK	hormonally up-regulated Neu-associated kinase (source: HGNC symbol; Acc.: 13326) (ENSOCUT00000005095)
A_04_P013035	0.02182632	-3.7424948	-1.9040003	3.7424948	Down	LBP	<i>O. cuniculus</i> LBP, mRNA (NM_001195719)
A_04_P057380	2.48E-04	-2.2619977	-1.1775975	2.2619977	Down	C12H6orf52	Predicted: <i>O. cuniculus</i> chromosome 12 open reading frame, human C6orf52 (C12H6orf52), mRNA (XM_008262518)
A_04_P087052	0.03150471	-2.5041976	-1.3243484	2.5041976	Down	CITED1	Cbp/p300-interacting transactivator, with Glu/Asp-rich carboxy-terminal domain, 1 (source: HGNC symbol; Acc.: 1986) (ENSOCUT00000013306)

Contd...

Supplementary Table 2: Contd...

Probe name	P (drug)	FC ([M-T] vs. [M-C])	Log FC ([M-T] vs. [M-C])	FC (abs) ([M-T] vs. [M-C])	Regulation ([M-T] vs. [M-C])	Gene symbol	Description
A_04_P034532	0.004731383	-2.0362408	-1.0259081	2.0362408	Down	LOC100355813	Predicted: <i>O. cuniculus</i> putative olfactory receptor GPCR LTM7 (LOC100355813), mRNA (XM_008269585)
A_04_P098432	0.006838933	2.5211353	1.3340735	2.5211353	Up	UGGT2	Predicted: <i>O. cuniculus</i> UGGT2, mRNA (XM_008260110)
A_04_P079622	0.04048189	2.453092	1.2946014	2.453092	Up	RIC8B	Predicted: <i>O. cuniculus</i> RIC8 GEFB (RIC8B), transcript variant X4, mRNA (XM_008257114)
A_04_P086674	0.035622377	2.7692554	1.4694982	2.7692554	Up	ARHGAP11A	Predicted: <i>O. cuniculus</i> Rho GTPase ARHGAP11A, transcript variant X1, mRNA (XM_008269248)
A_04_P065378	0.032835804	4.4598975	2.1570106	4.4598975	Up	ELOVL2	ELOVL fatty acid elongase 2 (source: HGNC symbol; Acc.: 14416) (ENSOCUT00000013015)
A_04_P080267	0.037696593	2.0473847	1.0337822	2.0473847	Up	HTR2B	5-hydroxytryptamine (serotonin) receptor 2B, G protein-coupled (source: HGNC symbol; Acc.: 5294) (ENSOCUT00000008577)
A_04_P001519	3.12E-04	-2.1444156	-1.1005845	2.1444156	Down	LPH	<i>O. cuniculus</i> LPH, mRNA (NM_001101689)
A_04_P001868	0.0339396	2.501716	1.3229179	2.501716	Up	ADH1A	<i>O. cuniculus</i> alcohol dehydrogenase 1A (class I), alpha polypeptide (ADH1A), mRNA (NM_001101704)
A_04_P069259	0.012302654	-2.1960154	-1.1348882	2.1960154	Down	SLC26A4	Solute carrier family 26 (anion exchanger), member 4 (source: HGNC symbol; Acc.: 8818) (ENSOCUT00000012637)
A_04_P084833	0.008474713	-2.0781624	-1.0553083	2.0781624	Down	MBIP	MAP3K12 binding inhibitory protein 1 (source: HGNC symbol; Acc.: 20427) (ENSOCUT00000017089)
A_04_P088707	0.031126112	-2.180206	-1.1244645	2.180206	Down	CLEC1A	C-type lectin domain family 1, member A (source: HGNC symbol; Acc.: 24355) (ENSOCUT00000016787)
A_04_P084834	0.008935675	-2.0264857	-1.01898	2.0264857	Down	MBIP	MAP3K12 binding inhibitory protein 1 (source: HGNC symbol; Acc.: 20427) (ENSOCUT00000017089)
A_04_P090269	0.041180246	4.945238	2.30604	4.945238	Up	SH3GL2	SH3-domain GRB2-like 2 (source: HGNC symbol; Acc.: 10831) (ENSOCUT00000001181)
A_04_P002343	0.04295296	2.191567	1.1319628	2.191567	Up	FKBP1B	<i>O. cuniculus</i> FKBP1B, 12.6 kDa, mRNA (NM_001082145)
A_04_P092610	0.003830259	-2.5908234	-1.3734107	2.5908234	Down	PPP3R2	Predicted: <i>O. cuniculus</i> protein phosphatase 3, regulatory subunit B, beta (PPP3R2), transcript variant X1, mRNA (XM_002708148)
A_04_P099507	0.037753712	-2.3505616	-1.2330055	2.3505616	Down	AIM1	Absent in melanoma 1 (source: HGNC symbol; Acc.: 356) (ENSOCUT00000013372)
A_04_P047002	0.02501037	5.10943	2.3531623	5.10943	Up	ASRGL1	Asparaginase like 1 (source: HGNC symbol; Acc.: 16448) (ENSOCUT00000005922)
A_04_P081409	0.043412738	-2.7950842	-1.4828918	2.7950842	Down	CNPY1	Canopy FGF signaling regulator 1 (source: HGNC symbol; Acc.: 27786) (ENSOCUT00000002453)
A_04_P033563	0.002682326	-3.0705657	-1.6185045	3.0705657	Down	LOC100144334	Uncharacterized protein (source: UniProtKB/TrEMBL; Acc.: G1SR31) (ENSOCUT00000006477)
A_04_P031751	0.003351042	2.4737735	1.3067133	2.4737735	Up	ATP2A1	<i>O. cuniculus</i> ATPase, Ca ⁺⁺ transporting, cardiac muscle, fast twitch 1 (ATP2A1), mRNA (NM_001089318)

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Supplementary Table 2: Contd...

Probe name	P (drug)	FC ([M-T] vs. [M-C])	Log FC ([M-T] vs. [M-C])	FC (abs) ([M-T] vs. [M-C])	Regulation ([M-T] vs. [M-C])	Gene symbol	Description
A_04_P084752	0.04975975	4.1212277	2.0430741	4.1212277	Up	GRIA3	Glutamate receptor, ionotropic, AMPA 3 (source: HGNC symbol; Acc.: 4573) (ENSOCUT00000000315)
A_04_P067483	0.027998285	-2.0428982	-1.0306172	2.0428982	Down	GPRC5D	G protein-coupled receptor, family C, group 5, member D (source: HGNC symbol; Acc.: 13310) (ENSOCUT00000015334)
A_04_P065748	0.026877979	-2.5302963	-1.3393064	2.5302963	Down	LOC100337897	Chromosome 3 open reading frame 20 (source: HGNC symbol; Acc.: 25320) (ENSOCUT00000030393)
A_04_P003601	3.92E-04	-2.5369635	-1.3431027	2.5369635	Down	RAG2	<i>O. cuniculus</i> RAG2, mRNA (NM_001171141)
A_04_P061073	0.034238487	2.232792	1.1588488	2.232792	Up	GPR155	G protein-coupled receptor 155 (source: HGNC symbol; Acc.: 22951) (ENSOCUT00000003686)
A_04_P076697	0.04242808	3.9715614	1.9897063	3.9715614	Up	CLCA1	Chloride channel accessory 1 (source: HGNC symbol; Acc.: 2015) (ENSOCUT00000004738)

Probe name	Sequence
A_04_P090206	GCAGGCGTTTAATGCCAAATTGCCAAACACCATGGATTACGACACGACCAAATTATGTAG
A_04_P087007	AAGAAAAGGGTCCCGTGCTACAGGGGCATAAGACACACGTCCAAATTTTGTTC AATTTTA
A_04_P090204	AGGCGTTTAATGCCAAATTGCCAAACACCATGGATTACGACACGACCAAATTATGTAGTT
A_04_P087010	AAGGGAAAAGATGCTCGAAGCTCAATCACAGGGGTCTATAGAATCATTTTACATAGAGTCC
A_04_P087008	AATCATTTTACATAGAGTCCAGAGGAAAAAGGCTTCGGAGAGTGGCCAGTAATGATGCT
A_04_P087009	TCAATCACAGGGGTCTATAGAATCATTTTACATAGAGTCCAGAGGAAAAAGGCTTCGGAG
A_04_P090205	CAGGCGTTTAATGCCAAATTGCCAAACACCATGGATTACGACACGACCAAATTATGTAGT
A_04_P087011	AGAACACATTGCAATAATCAAGGGAAAAGATGCTCGAAGCTCAATCACAGGGGTCTATAG
A_04_P089349	AAGACTGGAAGTATGTCGCCATGGTCATCGACAGGATATTCCTCTGGCTGTTTATTATCG
A_04_P000511	TAAAAATAATTCAGA AACTGACCTCAGCGGCGACTGGGGGAACTTGACAAGTACGTTT CACA
A_04_P095722	ACAAAACACTTCTATTACTTCGTACAGAGATGAACCTCATAGACCGCAAGGAGCTAGAGC
A_04_P000512	ATAAAAAATAATTCAGA AACTGACCTCAGCGGCGACTGGGGGAACTTGACAAGTACGTT CAC
A_04_P061367	AAGAACA AATTGTGTGTAGACACTGGAATGGAAGGAGACTGGTGTGGCCTTATTCCCGTT
A_04_P044995	TGCAGTGCCCATCTTGTTGCAATTTTGTGTGTTTATGGGCAATCATCATCTATCTA
A_04_P039523	TTATTTTATGGAACAGGCCTTGGAGTTTATCTCAGTTCAACTTTCTCACTTTCTCCGGGG
A_04_P095726	TGCTACAAACACTTCTATTACTTCGTACAGAGATGAACCTCATAGACCGCAAGGAGCTA
A_04_P000514	AAATAAAAAATAATTCAGA AACTGACCTCAGCGGCGACTGGGGGAACTTGACAAGTACGTT C
A_04_P003594	GAATTCAAAAACTGTTTTCTCTCACAGTCTGAGGAGACCCTGAGAAATGTTGTGGAGATG
A_04_P081503	TACAAGTCAAGGGCCGAGGCGAAACGAATGAAGGTGGCAAAGAATGCACAGAATATAAC
A_04_P002146	TTTTCCGGCTCACGCTGCGCACCCAGGAGGTGACAAGCCGCATACGCACCCAGAGTTTCT
A_04_P095723	TACAAACACTTCTATTACTTCGTACAGAGATGAACCTCATAGACCGCAAGGAGCTAGAG
A_04_P095724	CTACAAACACTTCTATTACTTCGTACAGAGATGAACCTCATAGACCGCAAGGAGCTAGA
A_04_P061519	TATGGAATG GCTGTGGTTCGAAGAAATTTCTGGTGTCTATATTGCGCCATCCTTCTAT
A_04_P000515	GAAAAATAAAAAATAATTCAGA AACTGACCTCAGCGGCGACTGGGGGAACTTGACAAGTACGT
A_04_P008321	AAGGTCTACATCAATGACTCGGTGGAGCTGAGCCAGAATGAGCAA AAGCTGGCGGCCTGG
A_04_P027308	ACATCATGTTTCGCTTCTTCCCTGACA AACTTCAAGGCTGAAGTGAAAATGGTCTTTGAGC
A_04_P089820	TTGGTGAACCTGAATTTCCATCAGTCCCTTACTGATGATCAGAAATTAGTGGCTGAGGGC
A_04_P019731	CAATTTTGCTTGCAGAAAGCTTGA AATAAAAACATGTCCCTTAACTACATTGCTATGGAA
A_04_P051957	TCTTATCTGACA AACTCAAGAAGCTTCCAGAATGTCCCTGTGCTTGGTCAAAGTGAAGCG
A_04_P077947	TAATGCCCTTACTGTGCACTGCGCTGTCCAACA AACTCGTCCCGATGGCTGCAGAAGAT
A_04_P027310	CTACATCATGTTTCGCTTCTTCCCTGACA AACTTCAAGGCTGAAGTGAAAATGGTCTTTGA
A_04_P099127	CCTTCGAAGATCCCCACGCCCCAGAGGAAATCACCTGCCAGCAAGTCTCAAAGAGATAG
A_04_P033412	TGGATGGTTCCATTTGCCATGGTTATAAGAGAGACAGGAAGCTCCAAACTGAAGCACTTC
A_04_P067484	TGAGGAGGATGTAGCA TTAAC TTCATATGGTACTCCCATTCAGCTGCAGACTGTTGATCC
A_04_P095725	GCTACAAACACTTCTATTACTTCGTACAGAGATGAACCTCATAGACCGCAAGGAGCTAG
A_04_P072427	TTCTAGAAAGGAAACTGTTGAGAGAAAATCATGAATCAGAAGAAAAGACTCCAAAGGTG

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Supplementary Table 2: Contd....

Probe name	Sequence
A_04_P080361	TCTGTTCCAGCACGTGGGCATACACTCGTCACTCCTTGGGAAAAGAACAATATTTCAAAGT
A_04_P087084	ACAGGAAAGTGACAGAGTACCTGTAGGAGGAATGGCAGATTTGAACTTCAAATTTCAAAA
A_04_P050163	AAGCCAGAAGAAGTGGACGATGAAGTGTCTATTCTCCACGATCACTAGTATTTCCAGAG
A_04_P004291	ATATGGATAACAAGGGAAGCAGCTTTCATCGGGTCATCAAGGATTTTCATGATCCAAGGAGG
A_04_P067977	GGCTCCAGCGTCAAGTTTGTCTCCACGACATCATCCAGCCGCAAGAGCTATAGGCACTAA
A_04_P072197	ACAGGACTGATGATGAACATAATTGGAGTCTTGTGTGTGTTTTTGGCGGTCAACACCTGG
A_04_P042687	TTCTTAAGAAGATCCCTGAGAGCCAAGTGGTGGAGTACCAGCTGCCAGCGGGAGTGTCT
A_04_P102467	TTTATAGTGTACGGCTTTGAAGTGGCATCTTGTATCACAGCTGCAACACAACGAGACTTT
A_04_P072430	TTGACGATTTATCGAACTCTAGATGATGAGTGGGATGCACTGCCATTACAGAAGTTTCA
A_04_P005044	ATTTCCGAAAAGCCACTCTGTAATCATGATGTCATCAGTAGAAAACAGTAGGCACAGCAGC
A_04_P073707	TCTCAAGGTGACTTTGATCCAGGGGCCAAGTTCCACATCCCTTCAAGTGTGCCTTACATC
A_04_P001576	AACAACATCCTGGTGTAGTGCAAGATCCAGGAGCTCAAAAACGTGGCTTTGTTTGAAGAG
A_04_P002261	TGACCCTTGACCTTTATCCTGAACCACAGCATATGCATGCCAGGCTGGGCACGAGGCTCA
A_04_P067467	GATGATACCTCATTGATGTGTCTTCTTTATCAGAGAAAAACGCCTCAGACAGTTTGTGA
A_04_P050162	GTGTTCTATTCTCCACGATCACTAGTATTCCCAGAGGCAGAAAACAGAAAGTGGACAATC
A_04_P072428	ATTGAGCATGTGCAAAAACCTTTATGATGGATTCCTAGAAGGGAAAACCTGTTGAGAGAAAAT
A_04_P072431	TTCAAACCTGAAGAAGTCTCAGCTACCAGCTTTGACGATTTATCGAACTCTAGATGATGAG
A_04_P068348	TGGTAGACAAATCCAGTATGTGGATACCAACACCTTCTCTTGGAAAATGTGCTGTCTA
A_04_P013032	GGATTCAATGTGGAGCTGTTGGAAGCTCTCTCAACTACTACATTCTCAACAACCTCTAC
A_04_P060608	TGTTTACAAGGGACATAAACAAGCCATGATGTGAGTGAGAAAACAGAAAGCAGGAACCTG
A_04_P088684	CAACAACATAAAGATGCCACCGAAAAGGGAGAAAACCTGAAGTCTCAGGAAATATTTCTAAAC
A_04_P096167	TATGTCTTAATTGACGCTGTGATTGGAACGATTGAGATTGCTGTCATCTGTGTGGTGGTC
A_04_P046043	AAAGACCAAAACAGATCCAGGAAAAATTTCTTCTACTCGTCTCATTTTCCAGAAAGACACAATG
A_04_P072429	TGGGATGCACTGCCATTACAGAAAGTTTCAATTGAGCATGTGCAAAAACCTTTTATGATGGA
A_04_P088407	ATCCCCTGGTCCACATTTGTGTATGCTTTTGCCAAATGTCGCGTATATCACTGCAATGTCC
A_04_P075700	GATGCTCATATTTACCTGAACCACATTGAGCCTCTGAAAACCTCAGCTTCAGCGAGAACCA
A_04_P062848	TCTAACCCAGGATCTGATGGTGTTCAGGGACTACAGGCACTAACAATGACAAATTCAGCA
A_04_P069025	TTATTATAAACGATGTGCTCGGTATTAACAAGGTTGGCAGTGAAGTCCACTGTGCTCACA
A_04_P066317	AATCACACAGGGACACAGTTCTTTGAAATTAAGAAGAGCAGACCTTGACAGGGCTGATG
A_04_P012981	TCCATTGGAACCTGCAGGTTTTGGTGCAGGAGGACAAGCCAGCATGTGTCTGCCACTCTG
A_04_P062593	GGTACTTAACAGGTATTTGGAATATGCCATCATGTATCTCCATTTGCTTTTAAATGAGAC
A_04_P075697	GAAGATTTTCAAGCTTGAAGGGTACAACCCACATCCAACCTATTAATAAATGGAGATGGCTGTT
A_04_P056382	AGATAACAGGTCAACAACCTAGGACAGAGGGACCTACCGGTCAGCATCACCTTCTGGGTG
A_04_P075699	CTCAGCTTACAGCGAGAACCAAGACCTTTCCCAAAGCTCAAAAATCTTCGAAAAGTTGAGA
A_04_P075047	TCTAAGGAAATCATCACCTTTTGGCAGGTATGCTCAGAAAATACCACATGCCATTACTAA
A_04_P064848	CTTCTCCCTGACATTCTGTGTTCCAGGTGCAGAACAAAGAACAAGAAAGAAAAAGAAATAG
A_04_P080600	ACTGCAATATACAAAGATGAACCTGGCTCATCGTATTTCTACACATCAGAATCTGTGGTA
A_04_P049942	CTTGCCAAAGAAGCTAAAAAGGAAGATTTACTTGAAGCTAGTACCTATCATGCAGCTAAG
A_04_P013965	AACAATAATGCATTTTGAACGACAGCGAGTGGGAACCTCTTTCTGTGCTCTCAATGTAC
A_04_P079624	GGACACAGACACTGAAGAATACAAAATGCAAAAACCAACATTAATCTTATCACTGGTCA
A_04_P042877	ATGGAGAAGGCACACGGACCCTTTGTACCAGGAAGGACCTGGAGGTAGTGGAGACAGAT
A_04_P040417	TAACACCATCGTACAGATGCTCGCGTGTGTGAACCTCGTGGTGGAGTTCTGGCTGGAGAA
A_04_P062478	ACAAGGACTGCTTGGTCTTCTGAGAATATGCTTTTACGCCTTCAATCTTGTGTGCTTAT
A_04_P054449	CGGGCAAAATCCCTACTACTCAGAAAGTTGAGCTCAATTTTCATCTCTGTTTTCTGGCCACAT
A_04_P005094	AAGAAGTAGTTTTGCGAACAACCTCTGCTTTGGGAAAATGTGGGTCCGTTCACTTTCTCTG
A_04_P088683	TTGAAAACCTGCTTTGGAGAAATACCATGAAGGCATTGAAAAGGCAACAGAGGAGTGTAT
A_04_P013087	GTAGGTAGAACTCTTCAAATCATTCTCTTTCTACCTCAAGTTTGTACCTTAGAGAT
A_04_P075049	GGGATCTGTTTGAATTTGTTAAAGGTGGACATTCATTTCCAGAAGACATAAACCTTTTC
A_04_P047767	GTGAAGGACATAGACATGTTTTCCATGTGTGAGCATCATCTGGTCCATTTGTGGGAAAAG
A_04_P075048	TATAGAATCCATTTGGATGTCTGTGCTAGCTTAGACGTGTGATTGCAGCACATGGCTTTTCT
A_04_P087172	TATTTATAAAATCTACTGTCTACCACAGTGAAGCGCAGTGCCTGGAGTCCCTACGA
A_04_P069977	TTTCTCCAAGCTGTGCATATGCCACAGTCACTTTCCGGGAAGGGACAGGGTGGAG
A_04_P087082	GACCTGAAAACAGAACTCATCATCGGAATTTCAAATGCAGAAGGTTTTGGACTTGAGTAA
A_04_P086101	CTTACGTAAAGAAAATTTGATACCTTTATTCCACTTGAGCCTTCCACAATCTCCCAACT
A_04_P101877	TGTGAATGCTGGGACGGATGGAATGGAATGCATGTGAAATCTGGCTTGGCACAGAATAT

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Supplementary Table 2: Contd....

Probe name	Sequence
A_04_P098065	CTTTCTTCACTGAGGGAGATAAACTTTGATGATAACCCTTTGCTGAGACCTCCAATGGAA
A_04_P020052	CTTGAATGATGTCAGTTGACTGTACTGTAATGTTGTATCAACTGAAATTGAATGTTTGCCT
A_04_P018421	AGAGGACAAAAATCCCTTCAAGGAGCTCAAAGGAGGCTGTGTGATTTTCATAAGGAAAAAA
A_04_P057677	AAGTATCGCTGGTTCGCCGTCTTCTACCTGATCTTCTTCTTCTTCTGATCCCGTTGTGCG
A_04_P101879	GACTGCGACAAGCATGAAGGACTCATCTGTACAGGGAATGGAATTTGTAAGTGTGGAAAC
A_04_P004576	ATCTTACAAGAGACAAGCCGAGGAAGCGGAGGAACAATCCAATGTCAACCTCTCCAAATT
A_04_P055525	AGAGCTTCCAACCTTTGGATAAAGAAGGGTCTGAGAAGAAGCTACTGGGGGAGAATTTAG
A_04_P005121	GTTTGCATGGCCTTCTGGTTCTCAGCTTATCTAAGTCCATCCTGTTGGTCAAATTCCTC
A_04_P070787	ACATACTCCATAGAAAATCCCAAGATGACTTCTGTAGTCTGAGCACTCAACAGAGCTA
A_04_P003182	CCTCCTTTTCTTACCATAGCATTTTGACATGCTTGAGGTATACACTGTAGCCTATTTTG
A_04_P070344	TCTATATCAAGCCAATTAAGTACAGAGGTTCTATCAGAAAAGGGAGACAAGCTGGGGACCC
A_04_P047768	TGTGAAGGACATAGACATGTTTTCCATGTGTGAGCATCATCTGGTCCCATTTGTGGGAAA
A_04_P006369	AAGTAAAGACCAGGTTCCAGAGTTAGGGGCCCTTACCTAAGAGAAAAAGCACAACCTGAAA
A_04_P062481	CTTACAGATTGTGAACCTTGATTCTACATACATGAATGATGATTCCATTTGGTCCCTCAA
A_04_P047771	GATTGTGAAGGACATAGACATGTTTTCCATGTGTGAGCATCATCTGGTCCCATTTGTGGG
A_04_P013034	GAGGATTCAATGTGGAGCTGTTGGAAGCTCTCCTCAACTACTACATTCTCAACAACCTCT
A_04_P101515	AGAAGAAGCCACTTGTCAAGAGAGAAAAGCCTGAAGAATTCCAGACCCGAGTTAGAAGAG
A_04_P086097	GTGTCCTTGCCAAACAGTTTTATTGCTTCTGGTGTCTTGGACTTCCAAGACAATCCTGA
A_04_P072187	AAGAACAACAAGAATATGGCCTTCAAGCTCAAGTCCAAGTCGTGCCATGACCTTCTGTG
A_04_P101880	CATTTGTTCTGCAGAAGAATGGTACATTTCCGGGGGAATCTGTGACTGTGATGACAGAGA
A_04_P012961	TACATGGTGCCTGGAAGAACCAGTTTCGACCATTACAGCAAGCAGGACCCTGCTCGGAC
A_04_P062762	ATCGAGAAAATCATCGGCTCCGGAGAGTCCGGGGAAAGTCTGCTACGGGTGGCTACGGGTG
A_04_P004386	TGATGGAAAAGTCTTCATTCATTTGTGCAACTACATCGAGCCCTGGGAGGATCTGTCTTT
A_04_P079312	AGAGCTATGCAACAAGATCACAAGCAGCTTAAAAGACCACCAGAGTAAGGGACAGGCTAT
A_04_P047770	ATTGTGAAGGACATAGACATGTTTTCCATGTGTGAGCATCATCTGGTCCCATTTGTGGGA
A_04_P072188	CAAGAACAACAAGAATATGGCCTTCAAGCTCAAGTCCAAGTCGTGCCATGACCTTCTGT
A_04_P034787	TTCCGGAAAATGATCAAGTTCACGACGGGAAAAGAACCTTCAACCCTTACGGCTTCTAC
A_04_P084832	CAAGTCTTGCTTAGAAAATCAAGAGAAAGCAGAATCCATGGCAACTCACCACCTTCCATGA
A_04_P050376	TCCTTTGTTACTTCAACCATAAGAGTTCCTGGAGACTGATTCTGACCCACTCTCTGCCA
A_04_P016399	CAAAAACCTTTGATGACTTCTCTGTTTGCCAATTCCGGAACCTGAAAAGGTTTGTCTCTC
A_04_P064617	AATAATATCAAGCTGATTGACTTTGGTTTGAGCAACTGTGCGGGGATCCTGGGTTACTCC
A_04_P013035	AGTCGGAGGATTCAATGTGGAGCTGTTGGAAGCTCTCCTCAACTACTACATTCTCAACAA
A_04_P057380	ACAATATATGGCAAAAAGTGAAGAACTCTACGATTCCCTCATGAAGTGTCACTGGCAGCC
A_04_P087052	GAGCTGTGGCTGGGGCAGAATGAGTTTGACTTCACTGCAGACTTTCGGTCTGGTTGCTGA
A_04_P034532	ATGAAGGTGGCAATGAGGAGAATATTCAGCCAGCTGCTGTGTTCCAGAAGTTGTTTTAA
A_04_P098432	CTGTTAGATCAGCTTGAAAGCAAGAAGAAAAATGCAATTTTAGCTCATGATGAAGTCTAG
A_04_P079622	AAACTTGTCAACATGCTTGATAAACTTTCCAGGAGAGCAGATGTGAAGGACCTGCACCAG
A_04_P086674	GGATGACCTGACTAATCATGATAATTTAAAGTCTGTTGTAATATAGGCTTTTCTGCTGG
A_04_P065378	TTCTTAAACTTCTATGTTTCAGACATACCAAAAAACGCCAAGGAAGAAAGATACGCAAGAG
A_04_P080267	ACACTTCTCTCACCAGAAAATGAAGGTGGCAAAACTGAAGAGCAAGTCAGTTATGTATAG
A_04_P001519	TTTTCTCTCATGCTGCTTGAGTCTGTGGCTTGGCGTTTTTATCATACGCATTGTGCAAG
A_04_P001868	GAAAAATAAATGAAGGATTTGACCTGCTTCGCTCTGGGAAGAGTATTCGGACCATCCTG
A_04_P069259	TTCTTTTGTACTGTCCACGACGCTATCCTCTATCTGCAGAACCAGGTGAAATCCACAAAAG
A_04_P084833	TTCAACCCCTCAGCAGAATTTACTGGCTGAACTTGATGAGAAAATTAGTGCCCTCA
A_04_P088707	AAGTGCTGGAATTTGCCATGCCTCAGAGCCACTCTGAGTTTTTCTACTTATTTGGACAG
A_04_P084834	TGGAAGGCATCTCTCCTGAATACTTTTCACTTATAAACTTTTCTGGAAAAAGAAGAAAAG
A_04_P090269	GAGGGTGATATCATCACTCACTAATCAGATTGATGAGAACTGGTATGAAGGGATGCTT
A_04_P002343	AACCTTTCAGTTCCGAATTTGGCAAAACAGGAAGTCATCAAAGGTTTCGAAGAAGGTGCAG
A_04_P092610	GGAAAATATCCTTTGAGGAATTCAGCACTGTGGTTAGAGGCCTGGAGTTCCACAAGAAAGT
A_04_P099507	GTATGATCAGAATCACATCCTCAACACCGTGAGCAAAGAGAAGTTAACACAGGTGTG
A_04_P047002	TAAACGGTGAAGTTGAAATGGATGCTAGTATCATGGATGAAAAAGAACTTCCACGGGAG
A_04_P081409	TAAAAGTTTCTACTTCTATTCCGATGCCTACAGACCTTTGAAATTCCGCTGTGAGACTAT
A_04_P033563	ATGCACAGCTCCAGAAGTTGAAAATGGAGTAAGAGTCAACAGGAAATAGGAGTTTATTTT
A_04_P031751	AGGGACAAGGCGACCGACTGAGCTCAGCTGCTTATTATTGAAAATAAACAACACAAGAG
A_04_P084752	AACTACGCGACATACAGAGAAGGCTACAACGTGTATGGAACAGAGAGTGTAAAGATCTAG

Contd...

Supplementary Table 2: Contd....

Probe name	Sequence
A_04_P067483	GAGGAGGATGTAGCATTAACCTTCATATGGTACTCCCATTTCAGCTGCAGACTGTTGATCCT
A_04_P065748	AATCCACCTCGGAAGTAGAGAAAAAGGCAAAACAACCTTGACATGGAGATGCGTCCTCTCA
A_04_P003601	GGTTCTGGGAAAATCTTGACTCCTGCCAAGAAATCCTTTCTTAGACGGTTGTTTGACTAA
A_04_P061073	AGATTTCTTCAAAAGAGCCCTGAACAGAGTCCTCCTGTTATTAATGCAAGCCCCGCCTAT
A_04_P076697	GTTACATTTTAAAAATTTGTGGAAGTGGGTGGGAGAATTACAGGTATCCCTAGGCTCA

ACE: Angiotensin I converting enzyme; PRLR: Prolactin receptor; PRKCZ: Protein kinase C, zeta; LBP: Lipopolysaccharide binding protein; CYP19A1: Cytochrome P450, family 19, subfamily A, polypeptide 1; GEF: Guanine nucleotide exchange factor; UGGT2: UDP-glucose glycoprotein glucosyltransferase 2; ARHGAP11A: Activating protein 11A; LPH: Lactase phlorizin hydrolase; FKBP1B: FK506 binding protein 1B; RAG2: Recombination activating gene 2; *O. cuniculus*: *Oryctolagus cuniculus*.

Supplementary Table 3: Altered genes induced by SXSM treatment

Differential protein summary					
Protein number	Representative accession	Gene	Species	Name	Log 115:114
55	gi 291394365	ACAA2	<i>O. cuniculus</i>	Predicted: 3-ketoacyl-CoA thiolase, mitochondrial (<i>O. cuniculus</i>)	0.328
17	gi 655884414	ACO2	<i>O. cuniculus</i>	Predicted: Aconitate hydratase, mitochondrial (<i>O. cuniculus</i>)	0.624
87	gi 291405797	ACSF2	<i>O. cuniculus</i>	Predicted: Acyl-CoA synthetase family member 2, mitochondrial (<i>O. cuniculus</i>)	0.308
33	gi 655885133	ACSS1	<i>O. cuniculus</i>	Predicted: acetyl-coenzyme A synthetase 2-like, mitochondrial (<i>O. cuniculus</i>)	0.484
29	gi 291402113	ACTN2	<i>O. cuniculus</i>	Predicted: Alpha-actinin-2 (<i>O. cuniculus</i>)	-0.404
1020	gi 655866030	ADK	<i>O. cuniculus</i>	Predicted: Adenosine kinase isoform X1 (<i>O. cuniculus</i>)	0.308
531	gi 655896110	ADPRHL1	Protein ADP-ribosylarginine	Predicted: (Protein ADP-ribosylarginine) hydrolase-like protein 1 (<i>O. cuniculus</i>)	-0.664
447	gi 655859663	AGT	<i>O. cuniculus</i>	Predicted: Angiotensinogen (<i>O. cuniculus</i>)	-0.440
4	gi 655882084	AHNAK	<i>O. cuniculus</i>	Predicted: Neuroblast differentiation-associated protein AHNAK isoform X8 (<i>O. cuniculus</i>)	-0.472
1372	gi 389886569	AKR1B10	<i>O. cuniculus</i>	Aldo-keto reductase family 1 member B10 (<i>O. cuniculus</i>)	-0.468
92	gi 42558920	ALDH1A1	RABBIT	RecName: full=Retinal dehydrogenase 1; Short=RALDH 1; Short=RalDHI; AltName: Full=ALDH-E1; AltName: Full=ALHDII; AltName: Full=Aldehyde dehydrogenase family 1 member A1; AltName: Full=Aldehyde dehydrogenase, cytosolic	-0.416
109	gi 655851269	ALDH4A1	<i>O. cuniculus</i>	Predicted: Delta-1-pyrroline-5-carboxylate dehydrogenase, mitochondrial (<i>O. cuniculus</i>)	0.328
199	gi 655862574	ANXA2	<i>O. cuniculus</i>	Predicted: Annexin A2 (<i>O. cuniculus</i>)	-0.300
132	gi 655601008	APOA1	<i>O. cuniculus</i>	Predicted: Apolipoprotein A-I isoform X1 (<i>O. cuniculus</i>)	-1.848
144	gi 284005104	APOA4	<i>O. cuniculus</i>	Apolipoprotein A-IV precursor (<i>O. cuniculus</i>)	-0.436
14	gi 655739959	ATP5B	<i>O. cuniculus</i>	Predicted: ATP synthase subunit beta, mitochondrial (<i>O. cuniculus</i>)	0.344
207	gi 291413480	ATP5H	<i>O. cuniculus</i>	Predicted: ATP synthase subunit d, mitochondrial (<i>O. cuniculus</i>)	0.384
466	gi 291411267	AZGP1	<i>O. cuniculus</i>	Predicted: Zinc-alpha-2-glycoprotein (<i>O. cuniculus</i>)	-0.480
923	gi 655838631	BASP1	<i>O. cuniculus</i>	Predicted: Brain acid soluble protein 1 (<i>O. cuniculus</i>)	-0.740
1203	gi 291411015	BCKDK	2721777.1	Predicted: [3-methyl-2-oxobutanoate dehydrogenase [lipoamide]] kinase, mitochondrial (<i>O. cuniculus</i>)	0.340
243	gi 291400445	BDH1	<i>O. cuniculus</i>	Predicted: D-beta-hydroxybutyrate dehydrogenase, mitochondrial (<i>O. cuniculus</i>)	0.336
582	gi 655815890	CALD1	<i>O. cuniculus</i>	Predicted: Caldesmon isoform X1 (<i>O. cuniculus</i>)	-0.492
154	gi 291384816	CAT	<i>O. cuniculus</i>	Predicted: Catalase (<i>O. cuniculus</i>)	-0.328
283	gi 655832713	CLYBL	<i>O. cuniculus</i>	Predicted: Citrate lyase subunit beta-like protein, mitochondrial (<i>O. cuniculus</i>)	-0.352

Contd...

Supplementary Table 3: Contd...

Differential protein summary					
Protein number	Representative accession	Gene	Species	Name	Log 115:114
461	gi 655897425	COX4I1	<i>O. cuniculus</i>	Predicted: Cytochrome c oxidase subunit 4 isoform 1, mitochondrial (<i>O. cuniculus</i>)	0.328
167	gi 655852771	CP	<i>O. cuniculus</i>	Predicted: Ceruloplasmin isoform X2 (<i>O. cuniculus</i>)	-0.668
208	gi 729207	CRYAB	RABIT	RecName: Full=Alpha-crystallin B chain; AltName: Full=Alpha(B)-crystallin	-1.024
505	gi 655833140	CTNNB1	<i>O. cuniculus</i>	Predicted: Catenin beta-1 (<i>O. cuniculus</i>)	-0.552
504	gi 655901408	CTSD	<i>O. cuniculus</i>	Predicted: Cathepsin D (<i>O. cuniculus</i>)	-0.368
178	gi 291398429	DBT	<i>O. cuniculus</i>	Predicted: Lipoamide acyltransferase component of branched-chain alpha-keto acid dehydrogenase complex, mitochondrial (<i>O. cuniculus</i>)	0.368
535	gi 655761595	DDX17	<i>O. cuniculus</i>	Predicted: Probable ATP-dependent RNA helicase DDX17 (<i>O. cuniculus</i>)	-0.356
424	gi 655840060	DDX39B	<i>O. cuniculus</i>	Predicted: Low quality protein: Spliceosome RNA helicase DDX39B (<i>O. cuniculus</i>)	-0.380
576	gi 913375	decorin	<i>O. cuniculus</i>	Decorin (<i>O. cuniculus</i>)	-0.412
210	gi 291383892	DLAT	<i>O. cuniculus</i>	Predicted: Dihydropyridyllysine-residue acetyltransferase component of pyruvate dehydrogenase complex, mitochondrial (<i>O. cuniculus</i>)	0.328
696	gi 655858948	ECHDC3	<i>O. cuniculus</i>	Predicted: Enoyl-CoA hydratase domain-containing protein 3, mitochondrial isoform X2 (<i>O. cuniculus</i>)	0.452
124	gi 291399590	ENO1	<i>O. cuniculus</i>	Predicted: Alpha-enolase (<i>O. cuniculus</i>)	-0.444
2070	gi 291394172	ENOSF1	<i>O. cuniculus</i>	Predicted: Mitochondrial enolase superfamily member 1 (<i>O. cuniculus</i>)	-0.516
322	gi 32363162	EZR	RABIT	RecName: full=Ezrin; AltName: Full=Cytovillin; AltName: Full=Villin-2; AltName: Full=p81	-0.412
103	gi 291401111	FGA	<i>O. cuniculus</i>	Predicted: Fibrinogen alpha chain (<i>O. cuniculus</i>)	0.584
204	gi 291401109	FGB	<i>O. cuniculus</i>	Predicted: Fibrinogen beta chain (<i>O. cuniculus</i>)	0.516
289	gi 655856160	FGG	<i>O. cuniculus</i>	Predicted: Fibrinogen gamma chain isoform X2 (<i>O. cuniculus</i>)	0.592
45	gi 284004982	FLNA	<i>O. cuniculus</i>	Filamin-A (<i>O. cuniculus</i>)	-0.408
490	gi 655835149	FLNB	<i>O. cuniculus</i>	Predicted: Filamin-B isoform X7 (<i>O. cuniculus</i>)	-0.300
1284	gi 655882129	FTH1	<i>O. cuniculus</i>	Predicted: Ferritin heavy chain (<i>O. cuniculus</i>)	-0.528
791	gi 655848679	FUBP1	<i>O. cuniculus</i>	Predicted: Far upstream element-binding protein 1 isoform X15 (<i>O. cuniculus</i>)	-0.344
276	gi 291416166	GSTP1	<i>O. cuniculus</i>	Predicted: Glutathione S-transferase P (<i>O. cuniculus</i>)	-0.324
476	gi 655733800	HNRNPA1	<i>O. cuniculus</i>	Predicted: Heterogeneous nuclear ribonucleoprotein A1 isoform X3 (<i>O. cuniculus</i>)	-0.384
864	gi 655887639	HNRNPM	<i>O. cuniculus</i>	Predicted: Low quality protein: Heterogeneous nuclear ribonucleoprotein M (<i>O. cuniculus</i>)	-0.516
986	gi 291406576	HSPA2	<i>O. cuniculus</i>	Predicted: Heat shock-related 70 kDa protein 2 (<i>O. cuniculus</i>)	-0.436
116	gi 291390901	HSPB1	<i>O. cuniculus</i>	Predicted: Heat shock protein beta-1 (<i>O. cuniculus</i>)	-0.428
18	gi 291391974	HSPD1	<i>O. cuniculus</i>	Predicted: 60 kDa heat shock protein, mitochondrial (<i>O. cuniculus</i>)	0.596
38	gi 291410533	IDH2	NADP	Predicted: Isocitrate dehydrogenase [NADP], mitochondrial (<i>O. cuniculus</i>)	0.632
1004	gi 291406081	KRT19	<i>O. cuniculus</i>	Predicted: Keratin, Type I cytoskeletal 19 (<i>O. cuniculus</i>)	-0.800
536	gi 655730920	KRT8	<i>O. cuniculus</i>	Predicted: Keratin, Type II cytoskeletal 8 (<i>O. cuniculus</i>)	-1.096
361	gi 291392980	LCP1	<i>O. cuniculus</i>	Predicted: Plastin-2 (<i>O. cuniculus</i>)	-0.532
158	gi 291404101	LDB3	<i>O. cuniculus</i>	Predicted: LIM domain-binding protein 3 isoform X4 (<i>O. cuniculus</i>)	-0.472
345	gi 655846237	LMNA	<i>O. cuniculus</i>	Predicted: Lamin isoform X1 (<i>O. cuniculus</i>)	-0.428
400	gi 655855761	LOC100339009	<i>O. cuniculus</i>	Predicted: ATP synthase-coupling factor 6, mitochondrial-like (<i>O. cuniculus</i>)	0.420

Contd...

Supplementary Table 3: Contd...

Differential protein summary					
Protein number	Representative accession	Gene	Species	Name	Log 115:114
196	gi 291386253	LOC100343793	<i>O. cuniculus</i>	Predicted: Cytochrome c oxidase subunit 5B, mitochondrial (<i>O. cuniculus</i>)	0.428
1135	gi 655885637	LOC100344952	<i>O. cuniculus</i>	Predicted: Histone H2B type 1 (<i>O. cuniculus</i>)	-0.488
1947	gi 655852407	LOC100345698	<i>O. cuniculus</i>	Predicted: Inhibitor of carbonic anhydrase-like isoform X1 (<i>O. cuniculus</i>)	-0.592
127	gi 655887883	LOC100346411	<i>O. cuniculus</i>	Predicted: Cytochrome c oxidase subunit 5A, mitochondrial (<i>O. cuniculus</i>)	0.432
549	gi 655839888	LOC100349084	<i>O. cuniculus</i>	Predicted: Histone H1.2 (<i>O. cuniculus</i>)	-0.504
1633	gi 655878767	LOC100349190	<i>O. cuniculus</i>	Predicted: Low quality protein: growth Arrest and DNA damage-inducible proteins-interacting protein 1-like (<i>O. cuniculus</i>)	0.344
108	gi 655831556	LOC100352842	<i>O. cuniculus</i>	Predicted: Alpha-2-macroglobulin (<i>O. cuniculus</i>)	0.312
940	gi 655831559	LOC100353846	<i>O. cuniculus</i>	Predicted: Alpha-2-macroglobulin-like isoform X1 (<i>O. cuniculus</i>)	-0.340
288	gi 291395803	LOC100354435	<i>O. cuniculus</i>	Predicted: Heat shock 70 kDa protein 1B-like (<i>O. cuniculus</i>)	-0.360
464	gi 655843262	LOC100357329	<i>O. cuniculus</i>	Predicted: Cytochrome c (<i>O. cuniculus</i>)	0.464
1105	gi 655602638	LOC100357801	<i>O. cuniculus</i>	Predicted: Interferon-induced very large GTPase 1-like isoform X2 (<i>O. cuniculus</i>)	0.356
297	gi 655901721	LOC100357978	<i>O. cuniculus</i>	Predicted: Low quality protein: EH domain-containing protein 1-like (<i>O. cuniculus</i>)	-0.300
129	gi 655837463	LOC100358789	<i>O. cuniculus</i>	Predicted: Low quality protein: dihydrolipoyl dehydrogenase, mitochondrial-like (<i>O. cuniculus</i>)	0.368
274	gi 307574681	LUM	<i>O. cuniculus</i>	Lumican precursor (<i>O. cuniculus</i>)	-0.652
6	gi 655603999	MYBPC3	<i>O. cuniculus</i>	Predicted: Myosin-binding protein C, cardiac-type (<i>O. cuniculus</i>)	-0.444
107	gi 655864030	MYH6	<i>O. cuniculus</i>	Predicted: Low quality protein: Myosin-6 (<i>O. cuniculus</i>)	1.052
1	gi 291403583	MYH7	<i>O. cuniculus</i>	Predicted: Low quality protein: myosin-7 (<i>O. cuniculus</i>)	-1.340
156	gi 291406966	MYL2	<i>O. cuniculus</i>	Predicted: Myosin regulatory light chain 2, ventricular/cardiac muscle isoform (<i>O. cuniculus</i>)	-1.008
149	gi 291393583	MYL3	<i>O. cuniculus</i>	Predicted: Myosin light chain 3 (<i>O. cuniculus</i>)	-0.560
478	gi 291401801	MYOZ2	<i>O. cuniculus</i>	Predicted: Myozenin-2 (<i>O. cuniculus</i>)	-0.392
539	gi 655601573	NCAM1	<i>O. cuniculus</i>	Predicted: Neural cell adhesion molecule 1 isoform X6 (<i>O. cuniculus</i>)	-0.472
720	gi 291389739	NDUFA12	2711251.1	Predicted: NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 12 (<i>O. cuniculus</i>)	0.428
474	gi 655898789	NDUFA13	8250959.1	Predicted: NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 13 (<i>O. cuniculus</i>)	0.488
814	gi 655645211	NDUFA2	2710300.2	Predicted: NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 2 (<i>O. cuniculus</i>)	0.396
722	gi 291411555	NDUFA7	2722046.1	Predicted: NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 7 (<i>O. cuniculus</i>)	0.716
931	gi 655878802	NDUFA8	8271654.1	Predicted: NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 8 (<i>O. cuniculus</i>)	0.424
193	gi 291392701	NDUFA9	2712902.1	Predicted: NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 9, mitochondrial (<i>O. cuniculus</i>)	0.436
956	gi 291383105	NDUFB6	2708084.1	Predicted: NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 6 (<i>O. cuniculus</i>)	0.344
63	gi 291392087	NDUFS1	<i>O. cuniculus</i>	Predicted: NADH-ubiquinone oxidoreductase 75 kDa subunit, mitochondrial (<i>O. cuniculus</i>)	0.340
258	gi 291384976	NDUFS3	2709147.1	Predicted: NADH dehydrogenase [ubiquinone] iron-sulfur protein 3, mitochondrial (<i>O. cuniculus</i>)	0.452
578	gi 655839067	NDUFS4	8260420.1	Predicted: NADH dehydrogenase [ubiquinone] iron-sulfur protein 4, mitochondrial (<i>O. cuniculus</i>)	0.456
794	gi 291399216	NDUFS5	2715247.1	Predicted: NADH dehydrogenase [ubiquinone] iron-sulfur protein 5 (<i>O. cuniculus</i>)	0.500

Contd...

Supplementary Table 3: Contd...

Differential protein summary					
Protein number	Representative accession	Gene	Species	Name	Log 115:114
318	gi 291394118	NDUFV2	2713628.1	Predicted: NADH dehydrogenase [ubiquinone] flavoprotein 2, mitochondrial (<i>O. cuniculus</i>)	0.524
527	gi 655848695	NEXN	<i>O. cuniculus</i>	Predicted: Nexilin isoform X3 (<i>O. cuniculus</i>)	-0.508
712	gi 75073382	OGN	RABIT	RecName: Full=Mimecan; AltName: Full=Osteoglycin; Flags: Precursor	-0.476
114	gi 291395294	OXCT1	<i>O. cuniculus</i>	Predicted: Succinyl-CoA:3-ketoacid coenzyme A transferase 1, mitochondrial (<i>O. cuniculus</i>)	0.400
155	gi 283549170	P4HB	<i>O. cuniculus</i>	Protein disulfide-isomerase precursor (<i>O. cuniculus</i>)	-0.384
213	gi 291393915	PDHB	<i>O. cuniculus</i>	Predicted: Pyruvate dehydrogenase E1 component subunit beta, mitochondrial (<i>O. cuniculus</i>)	0.324
232	gi 655603453	PDHX	<i>O. cuniculus</i>	Predicted: Pyruvate dehydrogenase protein X component, mitochondrial (<i>O. cuniculus</i>)	0.368
544	gi 655857157	PDLIM5	<i>O. cuniculus</i>	Predicted: PDZ and LIM domain protein 5 isoform X5 (<i>O. cuniculus</i>)	-0.396
965	gi 655600179	PLIN2	<i>O. cuniculus</i>	Predicted: Perilipin-2 isoform X2 (<i>O. cuniculus</i>)	-0.612
1041	gi 291409678	POSTN	<i>O. cuniculus</i>	Predicted: Periostin isoform X3 (<i>O. cuniculus</i>)	-0.472
228	gi 291404901	PRDX3	<i>O. cuniculus</i>	Predicted: Thioredoxin-dependent peroxide reductase, mitochondrial (<i>O. cuniculus</i>)	0.332
135	gi 291397244	PRDX6	<i>O. cuniculus</i>	Predicted: Peroxiredoxin-6 (<i>O. cuniculus</i>)	-0.372
493	gi 655899020	RCN3	<i>O. cuniculus</i>	Predicted: Reticulocalbin-3 (<i>O. cuniculus</i>)	-0.416
368	gi 291414084	SERPINA3	<i>O. cuniculus</i>	Predicted: Alpha-1-antichymotrypsin (<i>O. cuniculus</i>)	-0.400
278	gi 655868465	SERPINF2	<i>O. cuniculus</i>	Predicted: Alpha-2-antiplasmin isoform X2 (<i>O. cuniculus</i>)	-0.692
1859	gi 655604153	SF3B2	<i>O. cuniculus</i>	PREDICTED: splicing factor 3B subunit 2 (<i>O. cuniculus</i>)	-0.576
659	gi 655865891	SNCG	<i>O. cuniculus</i>	PREDICTED: gamma-synuclein (<i>O. cuniculus</i>)	-0.388
458	gi 655844284	SOD2	Mn	Predicted: Superoxide dismutase [Mn], mitochondrial (<i>O. cuniculus</i>)	0.392
1207	gi 655851673	STMN1	<i>O. cuniculus</i>	Predicted: Stathmin isoform X4 (<i>O. cuniculus</i>)	-0.520
146	gi 655880099	SUCLA2	ADP-forming	Predicted: Succinyl-CoA ligase [ADP-forming] subunit beta, mitochondrial isoform X1 (<i>O. cuniculus</i>)	0.324
363	gi 291386439	SUCLG1	ADP/GDP-forming	Predicted: Succinyl-CoA ligase [ADP/GDP-forming] subunit alpha, mitochondrial (<i>O. cuniculus</i>)	0.908
46	gi 291393975	SUCLG2	GDP-forming	Predicted: Succinyl-CoA ligase [GDP-forming] subunit beta, mitochondrial (<i>O. cuniculus</i>)	0.568
338	gi 291383827	TAGLN	<i>O. cuniculus</i>	Predicted: Transgelin (<i>O. cuniculus</i>)	-0.544
84	gi 655704650	TGM2	<i>O. cuniculus</i>	Predicted: Protein-glutamine gamma-glutamyltransferase 2 (<i>O. cuniculus</i>)	0.580
1656	gi 291403258	THBS1	<i>O. cuniculus</i>	Predicted: Thrombospondin-1 (<i>O. cuniculus</i>)	0.336
236	gi 291393813	TNNC1	<i>O. cuniculus</i>	Predicted: Troponin C, slow skeletal and cardiac muscles (<i>O. cuniculus</i>)	-0.648
157	gi 291392777	TPI1	<i>O. cuniculus</i>	Predicted: Triosephosphate isomerase (<i>O. cuniculus</i>)	0.360
200	gi 655892501	TRAP1	<i>O. cuniculus</i>	Predicted: Heat shock protein 75 kDa, mitochondrial (<i>O. cuniculus</i>)	0.404
3	gi 655828141	TTN	<i>O. cuniculus</i>	Predicted: Low quality protein: Titin (<i>O. cuniculus</i>)	-0.404
249	gi 655894873	WARS	<i>O. cuniculus</i>	Predicted: Tryptophan-tRNA ligase, cytoplasmic isoform X1 (<i>O. cuniculus</i>)	-0.312
8	gi 645985959		0	Chain A, crystal structure of leporine serum albumin in complex with naproxen	-0.396
902	gi 15420611		<i>O. cuniculus</i>	PKA catalytic subunit alpha (<i>O. cuniculus</i>)	-0.364
928	gi 349538		<i>O. cuniculus</i>	Glutathione S-transferase (<i>O. cuniculus</i>)	-0.356
609	gi 559973		<i>O. cuniculus</i>	Aldose reductase (<i>O. cuniculus</i>)	-0.332
24	gi 298544459		<i>O. cuniculus</i>	Unnamed protein product (<i>O. cuniculus</i>)	0.372

Contd...

Supplementary Table 3: Condt...

Differential protein summary

Protein number	Log 116:114	Log P value 115:114	Log P value 116:114
55	0.328	-5.299	-6.378
17	0.188	-9.196	-1.975
87	-0.256	-3.019	-0.149
33	0.204	-6.738	-4.083
29	-0.212	-6.730	-2.697
1020	-0.196	-1.493	-0.178
531	0.084	-2.558	-0.367
447	0.396	-1.569	-2.721
4	0.020	-15.654	-1.477
1372	-0.276	-1.375	-0.914
92	-0.224	-2.658	-0.716
109	0.336	-3.895	-2.504
199	-0.016	-3.142	-0.059
132	0.028	-3.097	-0.145
144	-0.204	-6.978	-3.467
14	-0.428	-2.757	-0.688
207	-0.032	-1.578	-0.295
466	0.216	-2.508	-1.466
923	-0.484	-3.666	-2.878
1203	0.180	-1.410	-0.650
243	-0.068	-2.253	-0.688
582	0.036	-3.998	-0.385
154	-0.056	-5.039	-0.136
283	0.044	-3.217	-0.515
461	-0.144	-1.641	-0.607
167	0.864	-1.682	-12.422
208	0.076	-1.878	-1.434
505	-0.268	-2.764	-1.444
504	-0.272	-2.422	-1.042
178	0.020	-3.010	-0.030
535	-0.100	-2.291	-0.471
424	-0.028	-1.475	-0.026
576	-0.176	-2.354	-0.429
210	-0.060	-3.624	-0.066
696	0.424	-1.965	-1.903
124	0.056	-3.234	-1.963
2070	-0.208	-1.398	-0.659
322	0.308	-2.380	-2.404
103	0.872	-4.441	-7.153
204	0.788	-3.570	-6.348
289	0.904	-5.325	-8.654
45	0.108	-7.676	-1.941
490	0.020	-1.833	-0.095
1284	-0.176	-1.597	-0.433
791	0.016	-1.584	-0.177
276	-0.164	-1.542	-0.831
476	-0.012	-1.307	-0.285
864	-0.184	-2.309	-0.725
986	-0.052	-2.180	-0.025
116	0.060	-2.987	-0.133
18	0.384	-9.784	-5.614
38	0.056	-4.168	-4.594
1004	0.064	-2.884	-0.200
536	-0.104	-5.187	-0.580
361	0.088	-4.075	-0.488
158	-0.296	-4.023	-3.094

Contd...

Supplementary Table 3: Condt...

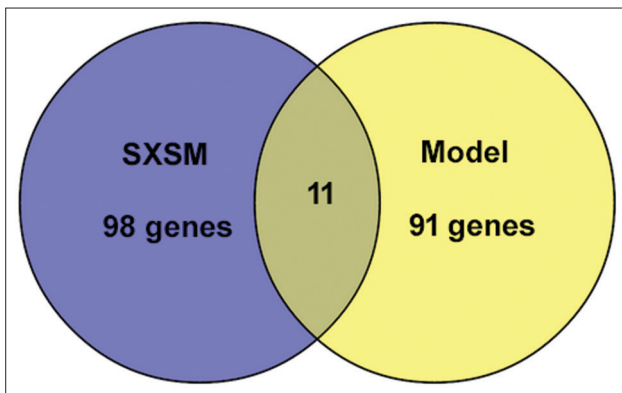
Differential protein summary			
Protein number	Log 116:114	Log P value 115:114	Log P value 116:114
345	-0.068	-4.225	-0.697
400	-0.016	-1.422	-0.063
196	-0.192	-1.807	-0.163
1135	-0.380	-1.542	-1.116
1947	-0.048	-1.363	-0.124
127	-0.372	-2.930	-0.097
549	-0.164	-2.058	-0.856
1633	-0.028	-1.382	-0.051
108	0.344	-3.940	-4.792
940	0.180	-1.617	-0.754
288	-0.012	-2.908	-0.500
464	0.264	-2.594	-0.886
1105	0.368	-1.830	-1.449
297	-0.124	-1.422	-0.240
129	-0.036	-2.069	-0.083
274	0.024	-5.601	-0.481
6	-0.348	-10.349	-8.247
107	0.768	-15.051	-5.832
1	-0.168	-16.000	-0.670
156	-0.388	-5.761	-0.790
149	-0.268	-4.539	-1.274
478	0.060	-3.140	-0.596
539	-0.180	-2.191	-0.784
720	0.068	-2.023	-0.104
474	0.116	-1.472	-0.303
814	0.240	-1.801	-1.141
722	0.428	-3.490	-1.483
931	0.332	-1.844	-1.209
193	0.000	-4.108	-0.010
956	-0.104	-1.638	-0.034
63	-0.120	-7.201	-0.027
258	0.100	-3.601	-0.636
578	0.144	-2.397	-0.482
794	-0.060	-1.382	-0.185
318	0.200	-2.701	-0.387
527	-0.164	-1.562	-0.448
712	-0.256	-1.540	-0.689
114	0.216	-6.595	-2.000
155	0.048	-3.904	-0.743
213	-0.076	-2.297	-0.078
232	0.152	-3.183	-1.091
544	-0.040	-1.537	-0.005
965	-0.284	-1.872	-0.616
1041	-0.372	-1.975	-1.702
228	0.100	-1.651	-0.417
135	-0.328	-2.082	-0.517
493	-0.024	-1.967	-0.075
368	0.404	-2.247	-3.156
278	0.268	-4.387	-4.529
1859	-0.428	-1.395	-1.544
659	-0.060	-1.973	-0.256
458	0.356	-1.927	-1.670
1207	-0.412	-2.092	-2.007
146	0.136	-3.076	-1.057
363	0.860	-2.041	-2.575
46	0.212	-3.211	-1.210
338	-0.024	-5.169	-0.009

Contd...

Supplementary Table 3: Condt...**Differential protein summary**

Protein number	Log 116:114	Log P value 115:114	Log P value 116:114
84	0.024	-8.826	-0.084
1656	0.460	-1.358	-1.907
236	-0.496	-4.662	-0.561
157	0.468	-2.575	-6.461
200	0.160	-1.696	-0.138
3	-0.092	-16.000	-0.727
249	0.064	-2.159	-0.597
8	0.192	-3.434	-5.032
902	-0.256	-2.069	-0.618
928	-0.036	-1.891	-0.077
609	-0.056	-1.450	-0.080
24	0.256	-1.471	-4.083

O. cuniculus: *Oryctolagus cuniculus*; CI: Confidence interval.



Supplementary Figure 1: Altered genes: A total of 11 genes were appeared in both model and SXSM originated differentially expressed genes.