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Original Article

Mesenchymal stem cells reverse thymus aging by reprogramming the DNA methylation of thymic epithelial cells

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ABSTRACT

Background: A decrease in the number and activity of thymic epithelial cells (TECs) is an important factor in thymic degeneration. Mesenchymal stem cells (MSCs) treating thymic ageing is a promising strategy, but the DNA methylation modification mechanism in TECs remains unclear.

Methods: Aged rhesus monkeys were treated with MSCs to establish a thymic senescence model, and hematoxylin-eosin (HE) staining, immunofluorescence staining, and ELISA were performed to observe the structure and function of the thymus. TEC aging model and MSCs co-culture system were established to detect DNA methylation modification and transcriptomic changes, correlation analysis between transcription factor methylation and mRNA expression, and q-PCR, immunofluorescence staining, and Western blot were used to identified key genes.

Results: MSCs improved the structure and function of thymus in elderly macaque monkeys; reduced the expression levels of β-Gal, P16, and P21; and increased the activity of aging TECs. There were 501 genes with increased methylation in the promoter region in the treated group compared with the untreated group, among which 23 genes were involved in the negative regulation of cell growth, proliferation and apoptosis, while 591 genes had decreased methylation, among which 37 genes were associated with promoting cell growth and proliferation and inhibiting apoptosis. Furthermore, 66 genes showed a negative correlation between promoter methylation levels and gene transcription; specifically, PDE5A, DUOX2, LAMP1 and SVIL were downregulated with increased methylation, inhibiting growth and development, while POLR3G, PGF, CHTF18, KRT17, FOXJ1, NGF, DYRK3, LRP8, CDT1, PRELID1, F2R, KNTC1 and TRIM3 were upregulated with decreased methylation, promoting cell growth.

Conclusion: MSCs improve the structure and function of aged thymus, which involves the regulation of DNA methylation profiles and a decrease in the methylation level of the transcription factor NGF to specifically upregulate KRT17 and FOXJ1 to promote the proliferation of TECs.

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1. Background

The thymus is the main lymphoid organ and is composed of thymic cells and thymic stromal cells. Thymic stromal cells include thymic epithelial cells (TECs), fibroblasts, dendritic cells and endothelial cells [1,2]. TECs are composed of cortical TECs (cTECs) and medullary TECs (mTECs). They maintain T-cell development at different stages through positive and negative selection, so TECs are an indispensable component of T lymphocyte maturation in the thymus [3,4]. However, in humans and mice, the thymus begins to

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degenerate after birth, and the reticular structure of the thymus epithelium is gradually replaced by adipose tissue, accompanied by a decrease in T-cell output [5,6]. Some experiments have shown that TECs have lower proliferation potential and that there is a higher percentage of apoptotic and senescent TECs in elderly animals, indicating that these cells may be a potential target for thymus rejuvenation therapy [7–9]. Therefore, the decrease in the number and activity of TECs may be the key factors related to the unfavorable changes in thymus structure and function in ageing.

The best way to reverse thymus ageing is to stimulate growth of the thymus, but this is a challenging scientific and technical problem involving developmental biology. Mesenchymal stem cells (MSCs) have multidirectional differentiation potential and immune regulation capability, secreting a variety of bioactive factors and playing important roles in inflammation, tissue damage repair and aging degeneration. In a study of a rhesus monkey aging model [10–13], we found that bone marrow MSCs (BMMSCs) derived from infant rhesus monkeys restored the structure and function of aging ovaries by promoting follicular and vascular regeneration, reducing the degree of ovarian fibrosis, and inhibiting apoptosis; improved lung structure and function by reducing fibrosis and inhibiting apoptosis, enhancing the division and proliferation of alveolar type II epithelial cells and improving their antioxidative stress ability; and significantly reversed the expression of age-related proteins in serum. In our previous study, it was also observed that MSCs could improve the structure and function of the thymus in elderly mice [14], but this observation needed to be confirmed with further studies in nonhuman primates, which are more closely related to humans. Moreover, the related cellular and epigenetic molecular regulatory mechanisms have not been clarified, leaving this an unanswered scientific question in the field.

DNA methylation is an epigenetic modification mode that regulates gene transcription without changing gene structure. It can turn gene transcription on or off through demethylation or methylation modification of specific genes and their promoters [15,16]. Previous studies have found that the high stability of DNA methylation is an important mechanism for stabilizing gene transcription, which regulates cell growth, division, proliferation, differentiation and secretory function by regulating gene opening and closing [17]. The methylation level of the functional gene itself is also closely related to the transcriptional expression of the gene, but whether it inhibits or promotes gene transcription is also related to the methylation site.

Therefore, we treated elderly macaques with MSCs and explored whether MSCs promote thymus tissue regeneration by acting on TECs in vivo; cocultured senescent TECs with MSCs to reveal the changes in genomic methylation and transcriptional profiles; and clarified the molecular regulatory mechanism to provide theoretical support for the use of MSCs in the treatment of thymic senescence.

2. Results

2.1. MSCs improving tissue structure and function of the thymus in elderly macaque monkeys

Elderly macaque monkeys aged 22–24 years old were treated with MSCs, which was injected into the femoral vein at a dose of 1×10^7/kg once every other day for a total of 3 times. The gross anatomy, morphology, tissue structure and function of the thymus were observed 5 months after the last treatment. In terms of thymus morphology and tissue structure, the results showed that the thymus tissue of elderly macaque monkeys obviously atrophied and degenerated and was replaced by a large amount of adipose tissue; the boundary of the cortical-medullary junction (CMJ) was blurred, and the number of thymocytes decreased. After MSC treatment, the thymus tissue regenerated, revealing that the volume of the thymus increased, the number of thymic epithelial cells, thymocytes and Hassall bodies increased, and the amount of adipose tissue decreased (Fig. 1A and B). In terms of thymus function, the thymus index and the levels of thymosin α and thymopoietin in peripheral blood were decreased, and the decreasing trend was reversed after MSCs treatment (Fig. 1C and D, Table 1). Finally, we detected the expression level of the aging marker gene P16 and the TEC marker molecule CK14 [18], and the results showed that P16 expression decreased, and the proportion of CK14 cells expressing the TEC marker molecule increased after MSCs treatment, (Fig. 1E and F). Those results implied that MSCs treatment improving the structure and function of aging thymus and promoting the regeneration of thymic lobules.

2.2. Intervention effect of MSCs on senescent TECs in vitro

To demonstrate that MSCs promote thymus tissue regeneration by promoting the growth and differentiation of TECs, we induced the senescence of TECs with 200 μmol/L H_2O_2 in vitro and cocultured MSCs with ageing TECs for 48 h in Transwells. Firstly, SA-β-gal (senescence–associated β-galactosidase, senescent cells appear blue due to increased β-galactosidase activity) staining showed that 55.3 ± 5.03% of the TECs in the induced senescence group were stained blue, and the number of blue cells decreased significantly after coculture (31.33 ± 7.03%) (Fig. 2A). Secondly, Dynamic observation by a Nanolive 4D microscope showed that MSCs secreted vesicles into the ageing TECs during coculture, which changed the volume of the TECs from large to small, and the loose nucleus became compact (Supplementary video 1). Then, under transmission electron microscopy, heterochromatin aggregation and patchy distribution were observed in senescent TECs, mitochondria were swollen, and no obvious autophagosomes were found in the cells. After coculture, the chromatin distribution of TECs was uniform, the mitochondria were still swollen, and a small number of autophagosomes could be seen in the cells (Fig. 2B). Next, western bloting and immunocytochemical staining were performed to detect the expression of the P16, P21 and Tunel protein, and the results showed that the expression of the ageing-related genes of P16, P21, and apoptosis increased significantly in the induced senescence group (1.59 ± 0.5, 1.17 ± 0.1, 85.66 ± 3.5%), and the expression of P16, P21 and Tunel was decreased after co-cultured with MSCs (1.14 ± 0.3, 1.10 ± 0.3, 33.06 ± 4.3%) (Fig. 2C and D). These results suggested that MSCs improve morphological structure and inhibit the expression of the aging markers SA-β-gal, P16, and P21, and decrease apoptosis to restore the growth of senescent TECs.

Supplementary video related to this article can be found at https://doi.org/10.1016/j.reth.2024.03.008

2.3. Changes in the genomic methylation profile in senescent TECs after MSCs coculture

To explore the intervention effect of MSCs on the whole-genome methylation modification profile of senescent TECs, we used whole-genome methylation sequencing (WGBS) to analyze the whole-genome methylation modification map of TECs after aging and MSCs coculture (Fig. 3A). The bioinformatics analysis method was used to conduct a series analysis of the WGBS database, resulting in 76.1 billion WGBS paired terminal readings (Table 2). The average alignment rate of clean WGBS reads mapped to the reference genome (BSMAP (version: 2.90) was 90.8%, and the coverage rate of the reference C base was 95%. We found that the average genome-wide methylation level of TECs in the induced

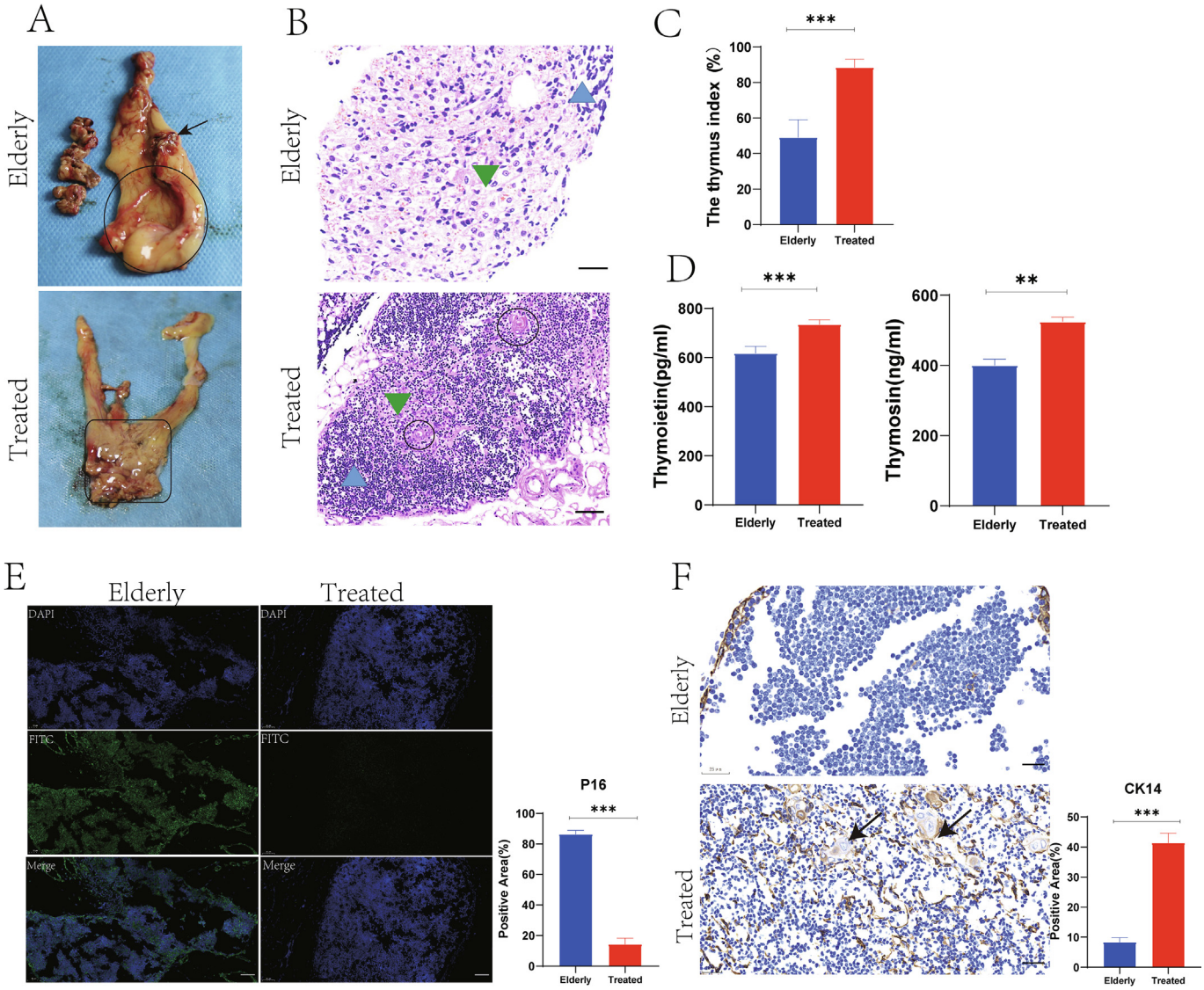

Fig. 1. MSCs treatment changed thymus morphology, tissue structure, secretory function, and P16 and CK14 expression in aged macaque monkeys. **A** Comparison of the appearance and morphology of thymus between the Elderly and the Treated: the above figure shows the appearance of thymus of the aged macaque monkeys, represents the area of adipose tissue in the thymus. The figure on the below shows the appearance of the thymus after MSCs treatment, and represents the thymus tissue area. **B** HE staining of thymus tissue from the senescent elderly group and treatment group (100×, ▲represents thymus cortex, ▼represents the thymus medulla; ◯ represents the Hassel body). **C** and **D** Comparison of thymus index and the contents of thymopoietin α and thymosin in the elderly and treatment group. **E** Expression of P16 in the elderly and treatment group (400×). **F** The expression of CK14 in thymus tissue was detected by immunohistochemistry (400×, brown indicates antibody-positive reaction) (the measured values represent the mean ± standard deviation (ˆX ± s) of three replicate experiments. **P < 0.01, ***P < 0.001).

Table 1
Thymus index.

Group	Thymus massx(g)	Macaque body weight (kg)	Thymus index (organ weight g per kg body weight)	Convert to percentage
Elderly1	2	5.3	0.377358490566038	37.7358490566038
Elderly2	2.8	5	0.56	56
Elderly3	3	5.6	0.535714285714286	53.5714285714286
Treated1	5	6	0.833333333333333	83.3333333333333
Treated2	5.2	5.8	0.896551724137931	89.6551724137931
Treated3	4.9	5.3	0.924528301886793	92.4528301886793

senescence group was 64.13%. After coculture, the average methylation level of TECs increased (Fig. 3B). In the site methylation level analysis, 57.58% of the CG sites in the induced senescence group were hypermethylated (methylation levels ranged from 70 to 100%). The proportion of hypermethylated CG sites increased after MSCs coculture, while the proportion of hypomethylated CG sites (methylation level <30%) decreased after MSCs coculture (Fig. 3C). Subsequently, we analyzed the methylation level around the gene body, and the methylation level decreased gradually in the upstream 1 kb region of the gene. A significant decrease in

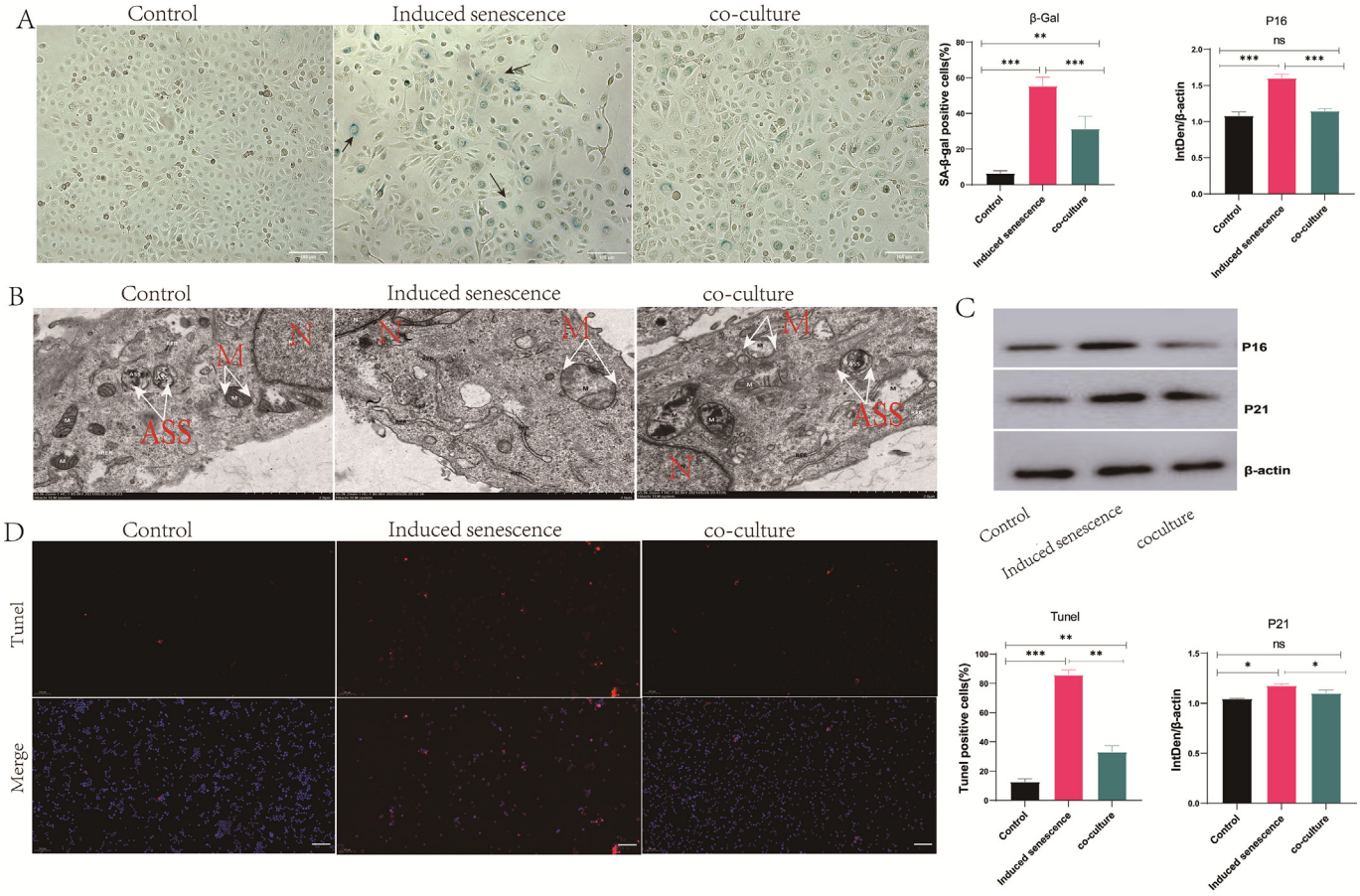

Fig. 2. Intervention effect of MSCs on aging TECs. **A** SA-β-gal staining of TECs after MSCs coculture (100 ×, represents increased activity of SA-β-gal). **B** Ultrastructural changes in TECs after MSC coculture (nucleus (N), mitochondria (M), and autophagosome (ASS); the upper scale is 2 μm). **C** After coculture with MSCs, the TEC senescence genes P16 and P21 were expressed. **D** TUNEL staining was used to detect the effect of MSCs on H_2O_2-induced apoptosis (the measured values represent the mean ± standard deviation (`X ± s) of three replicate experiments. *P < 0.05, **P < 0.01, ***P < 0.001).

methylation level was observed closer to the gene transcription start site (TSS). The methylation level in the gene body region was higher than that in the adjacent region and was relatively stable, while the methylation level in the transcription termination site (TTS) decreased significantly (Fig. 3D). Furthermore, the methylation changes in the TEC gene regulatory series after MSCs coculture were determined, and the annotations of senescence-related genes were extracted from the Gene Ontology Consortium (http://wiki.geneontology.org/index.php)). It was found that 1092 genes had methylation differences in the promoter region (Table 3). Among them, the methylation level in the promoter region of 501 genes was increased, and 23 genes were mainly involved in negative regulation of growth, proliferation and promotion of apoptosis. The methylation level of 591 genes decreased in the promoter region; 37 of these genes promoted cell growth, proliferation and anti-apoptosis (Fig. 3E and F) (Table 4). These results suggest that MSCs methylate the promoter region of genes related to apoptosis promotion, cell cycle arrest and growth inhibition in senescent TECs and turn off the expression of genes related to growth promotion, cell proliferation and apoptosis inhibition.

2.4. MSCs regulate gene transcription by inducing DNA methylation modification

To study the relationship between the DNA methylation modification pattern and gene transcription during MSCs reversal of TEC senescence, the genes in TECs were divided into four groups according to transcription level (high, medium, low and negative expression). We found that there was a negative correlation between DNA methylation and transcription in the promoter region (upstream 1 kb), a positive correlation between DNA methylation and transcription in the gene body region (Fig. 4A). In addition, the Pearson correlation coefficients (r) between DNA methylation levels and corresponding gene expression levels in the coculture group were calculated. The results also showed that DNA methylation levels in promoter and gene body regions were negatively correlated and positively correlated, respectively, with DNA methylation levels (Fig. 4B).

In the promoter region, after MSC coculture, 66 genes in senescent TECs exhibited a significant negative correlation between promoter methylation and transcription (Fig. 4C and Table 5). Methylation of PDE5A, DUOX2, LAMP1 and SVIL in the promoter region led to the downregulation of transcription. The expression of these genes mainly inhibited cell development, differentiation and the cell cycle. The demethylation of POLR3G, PGF, CHTF18, KRT17, FOXJ1, NGF, DYRK3, LRP8, CDT1, PRELID1, F2R, KNTC1 and TRIM3 in the promoter region led to an increase in transcriptional levels, and their expression mainly promoted the cell cycle, cell growth and development and epithelial cell differentiation (Fig. 4D). KEGG analysis showed that the genes with decreased methylation levels were mainly enriched in the Rap1 signaling pathway (Fig. 4E). Furthermore, the expression of key proteins RAP1, SRC and ITGB3 in the RAP1 signaling pathway was detected by Western blotting. The results showed that the expression of the key proteins RAP1, SRC

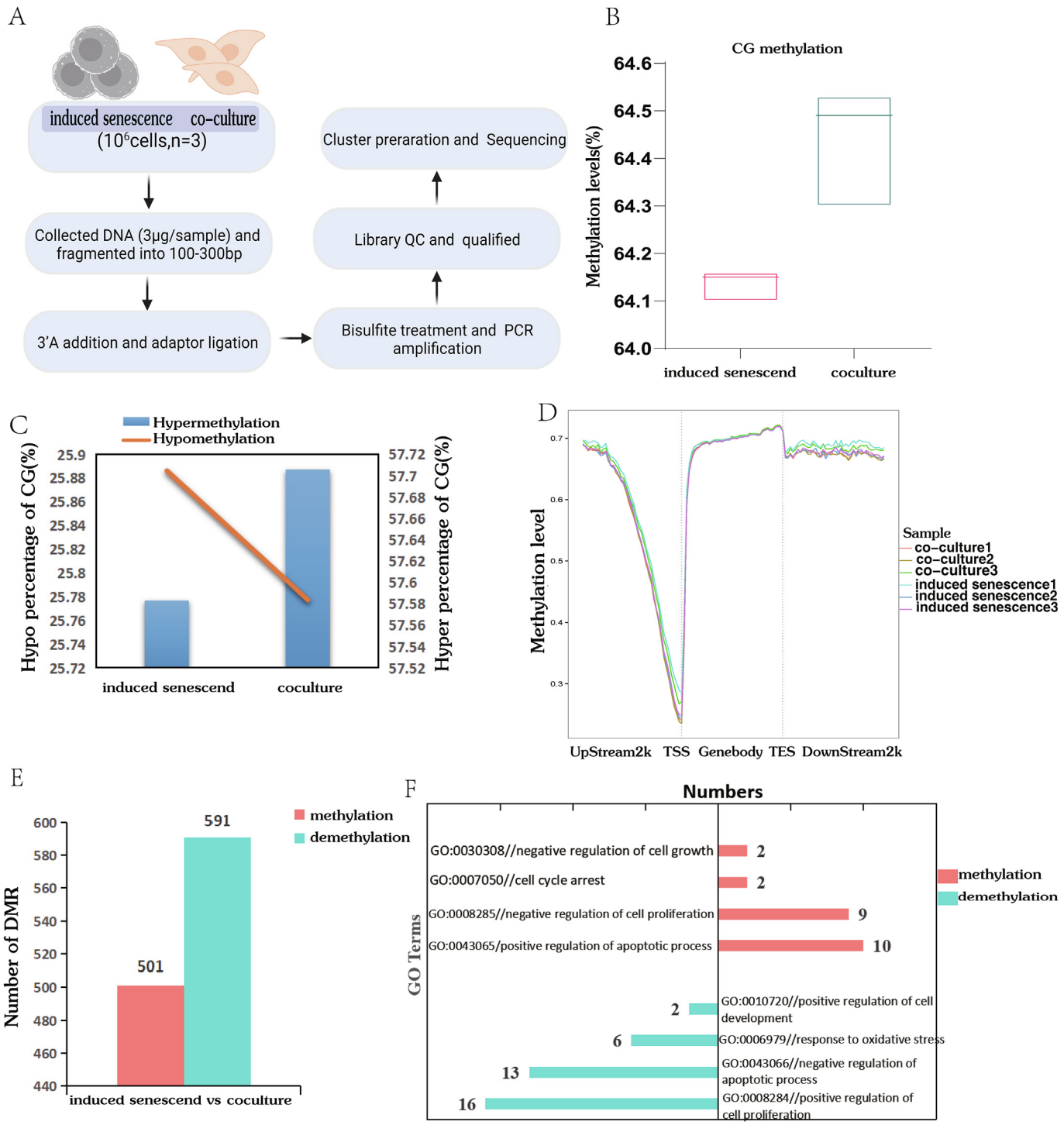

Fig. 3. Changes in the genomic methylation profile of senescent TECs after MSC coculture. **A** DNA methylation analysis workflow. **B** The average methylation level of the whole genome of senescent TECs after MSCs coculture. **C** The methylation level of CG loci in senescent TECs after MSCs coculture (orange lines indicate the percentage of low-methylated CG loci, blue histogram shows the percentage of hypermethylated CG loci). **D** DNA methylation levels at different locations of the gene (abscissa for different locations of the gene, ordinate for methylation level). **E** The differentially methylated genes in senescent TECs after MSCs coculture (red is the increase in methylation level, green is the decrease in demethylation level). **F** Enrichment analysis of ageing-related differentially methylated genes in TECs after MSCs coculture (the abscissa is the number of genes, and the ordinate is the GO name).

and ITGB3 increased significantly after MSCs coculture, suggesting that the decreased methylation of PGF and NGF activated the RAP1 signaling pathway (Fig. 4F). The results showed that MSCs induced a decrease in the methylation level in the promoter region of ageing-promoting genes, promoted the demethylation of cell growth gene promoters, inhibited the expression of ageing-promoting genes, promoted an increase in cell growth gene expression, and finally reversed the senescence of TECs. The

Table 2
Overview of WGBS and RNA-seq.

Sample	Basic data					Mapping_summary		Cytosines covgerage summary							
	Before filter Clean Data (bp)	After filter Clean Data(bp)	After filter Q20(%)	After filter GC(%)	BS Conversion Rate(%)	Mapped Reads	Mapped Ratio(%)	Cover_C_site	Coverage_C_rate(%)	Cover_CG_site	Coverage_CG_rate(%)	Cover_CHG_site	Coverage_CHG_rate(%)	Cover_CHH_site	Coverage_CHH_rate(%)
induced senescence1	129935007000.00	128996537171.00	96.44	21.14	99.1726	785756297	91.08	1139204604	94.99	54112170	92.2	241600401	95.26	843492031	95.1
induced senescence2	123296597700.00	122388023155.00	96.14	21.38	99.1842	743637765	90.84	1148446802	95.76	55009497	93.73	243620231	96.06	849817072	95.82
induced senescence3	121363978800.00	120054543421.00	96.38	21.38	99.153	723202127	90.06	1151420689	96.01	55225916	94.1	244218586	96.29	851976185	96.06
co-culture1	135175752300.00	134069766573.00	96.46	21.34	99.1876	816867744	91.01	1150752262	95.96	55194530	94.04	244111610	96.25	851446120	96
co-culture2	123507014100.00	122701110877.00	96.41	21.18	99.1815	748481642	91.23	1154482488	96.27	55464297	94.5	244859659	96.54	854158530	96.3
co-culture3	128602854900.00	127696268168.00	96.63	20.92	99.177	782219000	91.52	1142153850	95.24	54414238	92.71	242234242	95.51	845505368	95.33
Mean	126980200800.00	125984374894.17	96.41	21.2233333333333	99.1759833333334	766694095.833333	90.9566666666667	1147743449.16667	95.705	54903441.3333333	93.54666666666667	243440788.166667	95.985	849399217.666667	95.7683333333333
Total	761881204800.00	755906249365.00				4600164575									

Sample	Basic data				Mapping summary						sequenced_Total_Genes
	RawDatas	CleanData	AF_Q20(%)	AF_Q30(%)	Total_Mapped	Total_Mapped(%)	Unique_Mapped	Unique_Mapped(%)	Multiple_Mapped	Multiple_Mapped(%)	
induced senescence1	63242212	63106352	98.17	94.45	61526591	97.77	59881074	95.16	1645517	2.61	14728 72.57
induced senescence2	88342632	88112024	98.23	94.32	86149774	98.06	83834209	95.42	2315565	2.64	14879 73.31
induced senescence3	72322932	72143332	98.04	94.19	70243386	97.68	68278367	94.95	1965019	2.73	14829 73.07
co-culture1	68212998	68069126	98.09	94.33	66420866	97.84	64655493	95.24	1765373	2.6	14709 72.48
co-culture2	61494366	61382532	98.13	94.36	59913926	97.88	58267348	95.19	1646578	2.69	14661 72.24
co-culture3	61247622	61114060	98.06	94.24	59525003	97.66	57956113	95.09	1568890	2.57	14616 72.02
Mean	69143793.6666667	68987904.3333333	98.12	94.315	67296591	97.815	65478767.3333333	95.175	1817823.66666667	2.64	14737 72.615
Total	414862762	413927426			403779546						88422

Table 3
Differential methylation analysis.

id	meth.diff	meth.q
ENSG00000004534	11.1410214995872	0.0429895835444528
ENSG00000004534	13.2101994115724	0.0147077633344553
ENSG00000004660	12.8033744321869	0.0449216378457375
ENSG00000005206	11.9883161229276	0.00486888246659608
ENSG00000005206	16.4079172001707	0.000413089603869239
ENSG00000006611	32.9668348954578	0.0274261593096852
ENSG00000007171	19.2361927144536	0.0284955000718223
ENSG00000007264	21.036621036621	0.0247241716820028
ENSG00000007264	35.1750456280073	0.00800363463509878
ENSG00000010244	11.3078264865938	0.0127295348224089
ENSG00000011105	13.3912721893491	0.0370655291928072
ENSG00000025796	13.0936251519889	0.0253294671351397
ENSG00000025796	24.7747747747748	0.000261255054250883
ENSG00000027075	23.8587326822621	0.00152721677265883
ENSG00000027075	23.8587326822621	0.00152721677265883
ENSG00000028277	12.8211382113821	0.0417754562654187
ENSG00000035499	19.3525068415346	0.0442726305485908
ENSG00000048991	10.4895380349152	0.00234708565200044
ENSG00000056487	19.3288934426229	0.000346324136728837
ENSG00000057935	11.1359937892835	0.0216673574540229
ENSG00000064300	15.9053070905649	0.0313626607273396
ENSG00000065325	30.0664243639554	0.028033745947325
ENSG00000067225	14.5976635003821	0.000140304077436467
ENSG00000070087	12.0041443068912	0.000751864169014396
ENSG00000073146	28.3368254463589	1.79227087841047E-11
ENSG00000073670	13.6111807121579	0.0281038318353025
ENSG00000073849	15.5321329234373	0.0344241141481933
ENSG00000073861	14.2395496716356	0.0290369177541354
ENSG00000074211	31.0123456790123	0.0268393437770578
ENSG00000074219	11.9744703965236	0.00251060480696872
ENSG00000078124	21.7836257309941	0.0447363519040377
ENSG00000078549	24.8746457379551	3.10311426032942E-07
ENSG00000078549	19.6142930856553	3.5156097137167E-06
ENSG00000080371	14.5424394206038	0.00141882564824424
ENSG00000080845	12.6346909919374	0.029591386415805
ENSG00000083067	14.2926613616269	0.000291709269699351
ENSG00000083444	14.6650035637919	0.0276533853657112
ENSG00000083444	23.5729847494553	0.0147972826294937
ENSG00000083454	31.5746753246753	0.00664142162914082
ENSG00000088992	29.6296296296296	6.35666270161635E-07
ENSG00000088992	26.0344238002964	2.45996608894593E-08
ENSG00000088992	15.3504296759858	0.00698771447860245
ENSG00000089157	13.5674931129477	0.0398751044579701
ENSG00000089199	10.3386382673208	0.0247314804971351
ENSG00000089693	20.4041378101166	0.0169419692816553
ENSG00000091127	10.4413102820746	0.0474615788486051
ENSG00000091844	12.4604847207587	0.00656893745208257
ENSG00000092330	13.1012070566388	0.000153119337328558
ENSG00000092841	13.6121856866538	0.00589854211004375
ENSG00000095596	13.8338208211461	0.000133266843577669
ENSG00000095906	18.4410777507012	0.00106578761632672
ENSG00000096080	13.1624423963134	3.60710679412085E-13
ENSG00000099385	15.1779124333683	0.000505029650335907
ENSG00000099995	27.3128175630333	3.96812611779901E-05
ENSG00000100014	14.238574492658	0.00257404896789635
ENSG00000100038	36.9134363159429	3.7826902450755E-05
ENSG00000100147	18.4098639455782	0.0182070272285959
ENSG00000100209	15.8402203856749	0.000754006150568186
ENSG00000100288	28.4500466853408	0.00675645469505879
ENSG00000100344	33.1310942578548	0.0349828784568553
ENSG00000100739	23.1958939264328	0.00642102513264005
ENSG00000101057	11.4852240425329	0.027582108815626
ENSG00000101152	10.0759013282732	0.0183802377303916
ENSG00000101152	15.6436312692794	5.99465610526218E-08
ENSG00000101557	14.5645645645646	0.00498789412500717
ENSG00000101557	20.9821428571429	0.00296388715080506
ENSG00000101608	21.7574085059191	0.0119172703899002
ENSG00000101751	15.6150627615063	0.00847306283066711
ENSG00000102195	28.8316266577136	4.86516419633658E-05
ENSG00000102539	19.0187693038727	0.0241727783256494
ENSG00000103056	14.531033834334	0.0271381137967538
ENSG00000103089	23.6152005888848	4.1037077680861E-06
ENSG00000103197	13.6897001303781	0.0385416787972231
ENSG00000103260	34.8668280871671	0.00576313236691994

Table 3 (*continued*)

id	meth.diff	meth.q
ENSG00000104142	15.6246783986827	0.0355032569018309
ENSG00000104765	15.1990920268609	0.0215482067013419
ENSG00000104853	10.1353178509232	0.0182451782141719
ENSG00000105186	16.5007301208018	0.00452513955835274
ENSG00000105186	16.5007301208018	0.00452513955835274
ENSG00000106013	18.0428023785807	0.000524037914938989
ENSG00000106034	10.4788838612368	0.0288752690171604
ENSG00000106038	13.2367119708892	0.0116835243402002
ENSG00000106462	18.861272695223	0.000787825751585364
ENSG00000106689	12.1085577087978	0.0439548340409723
ENSG00000107551	10.7314782200305	0.0353103544330602
ENSG00000107831	16.358024691358	0.0329967000955916
ENSG00000107957	27.9484536082474	0.00724694443189657
ENSG00000108100	15	0.0336594557786585
ENSG00000108518	13.0415847497698	0.0355546305919269
ENSG00000108599	11.4219114219114	0.00649490868695054
ENSG00000108641	14.9391044088868	0.00674109795438447
ENSG00000108848	15.4737757171834	0.0352960887961454
ENSG00000108950	15.8198128545928	0.000286189101485006
ENSG00000109158	20	0.0374828243738455
ENSG00000109390	14.8784878487849	8.36294203163539E-05
ENSG00000109390	10.5591956919649	0.000460100120298561
ENSG00000109906	23.1024365352724	0.0024547054883833
ENSG00000109906	20.4666732955487	0.00140854131257951
ENSG00000110628	12.6218323586745	0.000905019819790039
ENSG00000110768	22.6938199415264	0.0266440194266571
ENSG00000110768	22.6938199415264	0.0266440194266571
ENSG00000111057	19.963963963964	0.000494478725805716
ENSG00000111057	16.6082144805549	0.0189635681399841
ENSG00000111271	14.5110267534346	0.0359526622537845
ENSG00000112312	14.2666860408796	0.000252933316932294
ENSG00000112312	12.0671851302075	0.00314034552387615
ENSG00000112539	19.8119889253751	0.0293719445323917
ENSG00000112837	15.3775922785966	0.00225950731419919
ENSG00000114026	16.5888093013599	0.000262572797788145
ENSG00000114026	12.4730430727983	0.0483647303353267
ENSG00000114405	17.9489421227487	0.0239681627595053
ENSG00000114978	14.891975308642	0.0277631947392702
ENSG00000114982	11	0.0237828902907722
ENSG00000115053	18.3673469387755	0.0345977207069055
ENSG00000115053	13.5922330097087	0.00228971892261384
ENSG00000115183	16.325731840605	0.00978959984261563
ENSG00000115507	14.2919726839325	2.65335702645699E-05
ENSG00000115507	16.5384896605359	7.80832598349621E-08
ENSG00000115596	19.7204968944099	0.0471322320159808
ENSG00000115596	18.5969387755102	0.0267926070508599
ENSG00000115648	12.9906661552231	0.000432032159732779
ENSG00000115648	11.4707653079293	0.00146399547053104
ENSG00000115657	20.1540832049307	0.0090588160999464
ENSG00000115839	15.513830002019	0.0282685367705523
ENSG00000115946	11.0898606987897	0.0151098790541535
ENSG00000116273	11.4664169119615	0.0291279908353443
ENSG00000117151	12.0481071754796	0.038042836527265
ENSG00000117597	23.6773179675223	0.00375105384414285
ENSG00000119004	16.7674418604651	0.0493690355960005
ENSG00000119547	13.0022197558269	0.0110827481784365
ENSG00000119547	15.0617079629279	0.00388583376741845
ENSG00000119547	24.4766505636071	0.000287897780947743
ENSG00000119599	11.9913818624387	0.0438215878070369
ENSG00000119953	12.8063228783438	0.0214469380195495
ENSG00000120063	27.1062271062271	0.000537666955164323
ENSG00000120063	28.0362443368224	1.64865091843957E-09
ENSG00000120063	24.7522457258766	0.00277354571261337
ENSG00000120088	25.1940719830628	0.00169770212477983
ENSG00000120215	11.0236220472441	0.006057045539393
ENSG00000120438	17.6411657559199	0.0197989462066386
ENSG00000121005	17.2958735733099	0.031629656826347
ENSG00000121210	20.8273208273208	0.0159666152087347
ENSG00000121236	17.0111238971998	2.8674824329256E-05
ENSG00000121236	17.4084595959596	0.000242040623929651
ENSG00000121314	21.285580231467	0.0498568351160869
ENSG00000121314	21.285580231467	0.0498568351160869
ENSG00000122545	11.8658149722696	0.00751222932209738
ENSG00000122545	13.4090447412523	3.84729012912294E-05
ENSG00000123999	19.0433862433862	0.0322288314190479

Table 3 (*continued*)

id	meth.diff	meth.q
ENSG00000124151	14.213317434417	0.0017111929157375
ENSG00000124275	11.5322171486555	0.0494296903067518
ENSG00000124782	15.0072481449055	0.0228088492132344
ENSG00000124785	26.3636363636364	0.0139015406017149
ENSG00000125046	21.9508196721311	0.000297526618890919
ENSG00000125046	22.159175750336	0.0041679258226915
ENSG00000125144	13.0402817859612	0.0436043261973361
ENSG00000126457	20.6477197620621	0.0436507205418902
ENSG00000126934	10.3994360902256	0.0170523230344648
ENSG00000127720	23.4776987718164	0.0497599820915567
ENSG00000128191	21.8181818181818	0.00320151574321917
ENSG00000128594	15.0125466477931	0.000116796230129294
ENSG00000128645	10.2853015529072	0.00121747150949854
ENSG00000128710	21.0644855381697	0.00651839107215014
ENSG00000129084	12.0286218655548	0.0172605152181004
ENSG00000129197	17.9736352881528	0.0417143548284744
ENSG00000130165	24.6307417627009	0.0160328131442227
ENSG00000130475	17.9204086677103	0.00166294018540342
ENSG00000130475	22.6388888888889	0.00604959086225118
ENSG00000130479	16.3249012522061	0.00953304964209787
ENSG00000130508	18.2250917171823	7.31610284271188E-06
ENSG00000130508	23.4640968662222	2.01088037520963E-06
ENSG00000130508	20.8543619322278	0.00416549842488869
ENSG00000130649	12.5517602327479	0.0273417480446
ENSG00000131016	11.7042662497208	0.0444354884016374
ENSG00000131023	13.9981479848311	0.0187010793104534
ENSG00000131351	13.4018264840183	0.00443589798182927
ENSG00000131477	33.4967320261438	0.0201872387865446
ENSG00000131558	11.5044247787611	0.022104739810866
ENSG00000132122	11.7731489585157	0.0277613788621418
ENSG00000132294	30.5308775731311	0.0327524240726326
ENSG00000132514	24.4631185807656	0.0363644555052197
ENSG00000132622	17.1397445984385	0.00566727737330212
ENSG00000132681	16.8425509738779	0.000928544009878355
ENSG00000132681	17.2377319230102	0.00203151969725212
ENSG00000132744	14.7559941407756	0.00904438540297216
ENSG00000132938	18.2909416035017	0.00125957506818755
ENSG00000132938	16.4396700556302	0.029970950411108
ENSG00000133067	11.3456085567639	0.0021492797615916 9
ENSG00000133124	28.093567251462	0.00327712188231578
ENSG00000133124	23.2823397075366	0.0020688231716342
ENSG00000133392	13.6334340382679	0.0376927615809148
ENSG00000133800	16.4758674298636	0.0269458437538327
ENSG00000134317	12.8983424355658	0.00952901638078628
ENSG00000134684	19.620253164557	0.0421639713050269
ENSG00000134684	13.9845510138397	0.0358154604847033
ENSG00000134759	20.113269661772	0.0003169386702829
ENSG00000135205	14.4243978386299	0.0176905740804252
ENSG00000135249	11.9803313524666	4.44647180285375E-06
ENSG00000135249	12.0194253338729	2.75460972867861E-05
ENSG00000135272	21.6901408450704	0.0287800161849221
ENSG00000135537	18.4814107312256	0.000239996476130441
ENSG00000135537	17.0307912883184	0.000260476898111422
ENSG00000135540	11.2881459231205	8.23366427538316E-06
ENSG00000135577	21.9239829785407	5.33522780546147E-07
ENSG00000135577	20.2328042328042	3.79900715392759E-05
ENSG00000135604	10.7653326403326	0.0439825159727086
ENSG00000135917	15.7698881460808	0.0366545557132403
ENSG00000135956	10.7649253731343	0.00292974515959743
ENSG00000136247	12.3814965295412	0.0274261593096852
ENSG00000136535	25.7446221731936	0.00370113043124773
ENSG00000136535	15.1667499681494	0.0203612063255517
ENSG00000136643	10.9614962348717	0.00659446668166033
ENSG00000136807	17.1372688477952	0.0266994300458006
ENSG00000136816	11.254543057831	0.0476060494941858
ENSG00000136834	16.5581622678397	0.0197267201252213
ENSG00000137273	11.5365398602283	0.0062040157982351
ENSG00000137273	11.6312366530771	0.00713523122493758
ENSG00000137404	11.3023930797029	0.0255540271725796
ENSG00000138336	21.8070362473348	0.000861502987558523
ENSG00000138336	12.8354483045559	0.0268464451559656
ENSG00000138356	13.7419056429232	0.000813164123944 5
ENSG00000138356	20.2985074626866	2.62625104704409E-05
ENSG00000138356	11.8725944161147	0.0229952158724666

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Table 3 (*continued*)

id	meth.diff	meth.q
ENSG00000138463	10.0793650793651	0.0195000911259593
ENSG00000138613	14.0350877192982	0.0479560323476768
ENSG00000138735	16.2222222222222	0.0350319355454426
ENSG00000139218	10.8035714285714	0.0127859426977211
ENSG00000139436	11.7431596386322	0.016830731218501
ENSG00000139531	10.9577133507184	0.0139832071913536
ENSG00000139684	11.1080973047053	0.00994668784188908
ENSG00000140022	24.9410840534171	0.0476852247868617
ENSG00000140022	24.9410840534171	0.0476852247868617
ENSG00000140105	14.2249740905105	0.0439334492861912
ENSG00000140262	14.8026315789474	0.0180323921064519
ENSG00000140274	11.3766298330057	0.0425112978457713
ENSG00000140279	11.3766298330057	0.0425112978457713
ENSG00000140374	12.4095416778344	0.0295742567787071
ENSG00000140374	10.4160259004452	0.0212023889404258
ENSG00000140379	12.9888127393671	0.00146289741517831
ENSG00000140379	10.8886346300534	0.0143709320741482
ENSG00000141002	22	0.000139314238757079
ENSG00000141293	11.9499343227696	0.026388087032707
ENSG00000142279	17.6991150442478	4.44499535952698E-05
ENSG00000142534	11.3208047990657	0.0143487834433811
ENSG00000142538	18.8744588744589	0.0217087371662691
ENSG00000142552	18.1228934404978	0.023175861526316
ENSG00000142675	11.9416498993964	0.0438155979904791
ENSG00000142700	18.23190607602	1.52116319460919E-07
ENSG00000142700	22.2227505051706	3.15609809571843E-06
ENSG00000142700	12.4779239802585	0.000217406168500081
ENSG00000143367	11.9555984555985	0.000671624021843253
ENSG00000143398	15.7577990665684	0.0214919289811714
ENSG00000143398	13.6726096441736	0.00772983254202307
ENSG00000143398	11.6687495014491	0.0124536348395854
ENSG00000143412	12.5132555673383	0.0244041195439192
ENSG00000143858	28.140350877193	0.0449309937694186
ENSG00000143924	13.7603049375055	0.0407591408789525
ENSG00000144214	34.1558441558442	0.0284955000718223
ENSG00000144893	16.9635493979878	0.0306995524670432
ENSG00000145113	13.5961321012204	0.024083299094284
ENSG00000145536	15.5727366159021	0.0089577681604829
ENSG00000145592	11.6523025372436	0.0271636234060285
ENSG00000145757	13.6798764796706	0.0111201292225156
ENSG00000145779	13.0333463762445	0.0105378918259197
ENSG00000145779	16.1732764862038	0.000880696185937804
ENSG00000145936	24.8277559055118	0.0191371062416153
ENSG00000145945	17.0379193964662	0.017110700640367
ENSG00000146352	17.4763922571934	0.00939974597671166
ENSG00000146409	35.5370132648695	1.40578884203656E-09
ENSG00000146409	55.8620689655172	2.89770438201437E-13
ENSG00000146433	16.5959453088166	0.04996939925385
ENSG00000146576	11.163315696649	0.0311238715775918
ENSG00000146670	18.8444463416716	0.0367317352416859
ENSG00000147416	21.3716108452951	0.0105920429195674
ENSG00000147416	17.9113018597997	0.0474615788486051
ENSG00000148513	25.0413343002175	0.00269005183248194
ENSG00000148704	11.9206939281289	0.0253072631085157
ENSG00000149054	15.5116844162118	0.016766001714366
ENSG00000149506	15.5555555555556	0.000333635726247543
ENSG00000149506	15.3865286262805	4.96739707996025E-06
ENSG00000149527	29.7297297297297	0.00415449304741765
ENSG00000149527	29.7297297297297	0.00415449304741765
ENSG00000149639	10.9286870262367	0.0101548299807206
ENSG00000149639	12.1855383969921	0.0160852095767229
ENSG00000150281	15.1779124333683	0.000505029650335907
ENSG00000150394	26.9042103828859	0.0227936744086682
ENSG00000150394	27.0412642669008	0.0202594079795574
ENSG00000150712	12.5114453891432	0.0122139770215577
ENSG00000150712	10.867677850978	0.0214739383140781
ENSG00000150873	19.8901098901099	0.0405200413725175
ENSG00000151025	20.8704311152765	0.0202546161115284
ENSG00000151572	22.7093641194796	0.000482091129609184
ENSG00000151572	19.3722868352021	0.000468330770938237
ENSG00000151572	23.7637362637363	0.000220689154440144
ENSG00000151715	13.2231404958678	2.07242441821259E-05
ENSG00000151892	12.1728903263746	0.00735053012870515
ENSG00000151952	15.5023286759814	0.046398850179932

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Table 3 (*continued*)

id	meth.diff	meth.q
ENSG00000152056	19.958988380041	0.0198480823550037
ENSG00000152270	12.0286218655548	0.0172605152181004
ENSG00000152767	43.3974358974359	0.00117296285928984
ENSG00000152784	13.3333333333333	0.0231940237759357
ENSG00000153044	14.8214009587135	0.0216533179341455
ENSG00000153064	33.8714590313737	0.0495018361148693
ENSG00000153207	10.2739726027397	0.0026938679402231
ENSG00000153993	18.8775510204082	0.0241209264996128
ENSG00000154237	23.0392156862745	0.0363291714716197
ENSG00000154760	15.1098628310425	0.0347986539044008
ENSG00000154856	12.5283446712018	0.00037602103468744
ENSG00000154917	13.8822434875066	0.0230621445524481
ENSG00000155886	19.5566361556064	0.0116155325394393
ENSG00000156076	11.0310823222313	0.0268796003918146
ENSG00000157538	15.0242571255306	0.00203121890774945
ENSG00000157766	15.0971621989181	0.00676995036797155
ENSG00000157766	12.5436141184755	0.00464440476763111
ENSG00000157851	16.7903733693207	0.0289398471369681
ENSG00000158106	12.4241021843762	0.0188313265083686
ENSG00000158258	19.1297901887926	0.00225261451838968
ENSG00000158473	11.0937760919869	0.0128090642870108
ENSG00000158497	11.1524313836453	0.0150878523101572
ENSG00000158578	56.8181818181818	0.0336364256100912
ENSG00000158578	56.8181818181818	0.0336364256100912
ENSG00000160213	24.7969090548841	0.0122376863994378
ENSG00000160218	19.3254265056808	0.0133364009262115
ENSG00000160352	24.7552447552448	0.0295173147012498
ENSG00000160352	23.5333087964667	0.00337460458680132
ENSG00000160396	14.1804407713499	0.0211463722081773
ENSG00000160957	15.3463203463204	0.0486141677182154
ENSG00000161204	25.6061169104647	8.31439836576701E-07
ENSG00000161204	13.7002182214948	0.0473029553225241
ENSG00000161270	28.8167770419426	0.000660996990069051
ENSG00000161270	19.0286206954846	0.000119598769573488
ENSG00000161277	19.8897168020455	8.75707968258849E-08
ENSG00000161277	23.7220969376083	3.0737873482305E-10
ENSG00000161940	15.4950032850375	0.0139482207896637
ENSG00000162385	12.0503936791575	0.000736637004004158
ENSG00000162650	12.1210093032595	0.030390884371614
ENSG00000162650	10.6566159389371	0.0107260867722815
ENSG00000162669	38.9926183239253	0.0271186450532488
ENSG00000162670	24.0847486704409	0.00013024571749572
ENSG00000162670	20.3247232472325	0.000579881644268407
ENSG00000162745	13.1313131313131	0.0136091156485706
ENSG00000162745	13.1313131313131	0.0136091156485706
ENSG00000162972	14.4257014957965	0.0186020820238185
ENSG00000163040	14.046926910299	0.000944854924481721
ENSG00000163126	20.1949317738791	0.0481825564972396
ENSG00000163159	15.7577990665684	0.0214919289811714
ENSG00000163159	13.6726096441736	0.00772983254202307
ENSG00000163444	15.3428899552931	0.0196806547786023
ENSG00000163531	17.5438596491228	0.00676389422859917
ENSG00000163719	12.999359111301	0.000112140354846795
ENSG00000163749	65.1083591331269	8.36339221793695E-08
ENSG00000163884	15.0589955100762	0.0428100098509375
ENSG00000163888	13.1516566237808	0.0186911733603567
ENSG00000164111	14.0333333333333	0.0282875420942757
ENSG00000164362	13.683310187527	5.87564337928306E-05
ENSG00000164694	21.9051799824407	0.0303086708577827
ENSG00000164694	18.1836945304438	0.00134095427583391
ENSG00000164920	13.8862559241706	0.00141583621004862
ENSG00000165238	24.0134453781513	0.00494478632453144
ENSG00000165379	13.6731125022176	0.0016025149040758
ENSG00000165480	13.5407905803196	0.0216946706962642
ENSG00000165606	19.1199183733706	5.5872052215603E-07
ENSG00000165606	17.3925998740535	4.2808694077257E-05
ENSG00000165934	18.75	0.00971460786186196
ENSG00000165966	10.0216919739696	0.0305898143328863
ENSG00000166126	35.6637863315004	0.00259242502228986
ENSG00000166183	24.2622180451128	0.0190593482630599
ENSG00000166347	13.769569637411	0.0403563026530201
ENSG00000166477	15.1330878013432	0.00123670273324628
ENSG00000166477	12.283264834318	0.015419621646927
ENSG00000166501	19.6266805146847	0.00153775224272866
ENSG00000166573	17.4718111346018	0.00729498953313671

Table 3 (*continued*)

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ENSG00000166707	20.0104529616725	0.00163780758425276
ENSG00000166707	20.0104529616725	0.00163780758425276
ENSG00000166823	26.8245838668374	0.0495363996427847
ENSG00000166920	16.5035117421258	0.00589449445291069
ENSG00000166923	14.9973367002703	0.00447230701951687
ENSG00000166923	33.1261645269149	1.25223166306352E-10
ENSG00000166963	20.3389830508475	0.0300087921518017
ENSG00000167065	11.2352309344791	0.0139136993223702
ENSG00000167157	25.9079443434864	0.000277416303600727
ENSG00000167232	19.6491228070175	0.0476188588590909
ENSG00000167461	13.3822689555548	0.0371522468391887
ENSG00000167461	20.9423888008136	6.06355227548763E-05
ENSG00000167525	10.1274599061559	0.0152810805363086
ENSG00000167721	14.9361391296875	0.00380753155245858
ENSG00000167861	25.9545923632611	0.00358556744024635
ENSG00000167941	11.7389526051318	0.0285708560755144
ENSG00000168003	29.6517223220933	1.10573298130736E-15
ENSG00000168003	19.3742150067451	4.26219762277615E-18
ENSG00000168310	20.4081632653061	0.0279896116071751
ENSG00000168412	17.3148504684893	0.000716521181689353
ENSG00000168418	14.3181818181818	0.0182567992005783
ENSG00000169026	18.6301369863014	0.0342770267372644
ENSG00000169223	12.2437275985663	0.0435324183677553
ENSG00000169375	10.4188521863726	0.016114367702584
ENSG00000169393	12	0.0493167198534707
ENSG00000169427	11.247220890187	0.0496254884892535
ENSG00000169760	17.5231031128405	0.0186654039857985
ENSG00000170145	10.5361665414266	0.0175465943593796
ENSG00000170185	29.4871794871795	0.000630400715875306
ENSG00000170465	12.962743471218	0.0469277428773242
ENSG00000170561	12.7706888335892	0.0391539116619081
ENSG00000171100	22.871835443038	0.0106092170610959
ENSG00000171126	11.1359937892835	0.0216673574540229
ENSG00000171311	13.8118664281455	0.0237183365918712
ENSG00000171311	14.3968033579405	0.00413581751691176
ENSG00000171320	10.3273952816562	0.0167954591819699
ENSG00000171502	23.609756097561	0.0335180537417258
ENSG00000171680	13.5460627895008	0.00929318330919313
ENSG00000171703	14.2619545269168	0.00131329403970655
ENSG00000171863	11.5938898723481	2.56390100406467E-10
ENSG00000172020	42.5376344086022	0.000695352188831056
ENSG00000172020	24.2295293359123	0.047280709287646
ENSG00000172264	10.5454049631852	0.028981547758041
ENSG00000172375	22.5297619047619	0.00867841999556837
ENSG00000172638	14.5147565340717	0.0381796105921428
ENSG00000172731	11.4101485842445	0.00944905513209447
ENSG00000172969	11.7578638155014	0.044921147652781
ENSG00000173093	24.06191369606	0.022181003499463
ENSG00000173120	14.2551674982181	0.0496394849462093
ENSG00000173200	10.8415600053979	0.0320176211096451
ENSG00000173200	15.7881024750326	0.00412154700403832
ENSG00000173992	22.1199059561129	0.00699934725544673
ENSG00000174013	13.9814282192456	0.0394900528618909
ENSG00000174567	27.1601770479184	0.000340861700810797
ENSG00000174600	15.6376618349176	0.00642989573367869
ENSG00000175155	22.7486965589155	0.0111237785068831
ENSG00000175164	24.4719418821125	0.00013283575228985
ENSG00000175262	35.1402458241412	0.000497173920808733
ENSG00000175334	11.5209950030916	0.00625243526719106
ENSG00000175334	18.6723832789092	4.64281096741 43E-13
ENSG00000175334	14.2765027897673	0.00241994485726501
ENSG00000175548	14.4444444444444	0.00890661766993383
ENSG00000176533	13.5220678740988	0.00373615812375045
ENSG00000176635	16.6083998306865	0.000355215220754848
ENSG00000176697	14.5359848484848	4.5109359222386E-08
ENSG00000176884	22.6031645486097	2.01796375984741E-06
ENSG00000177453	14.4259397990741	0.035363394156332
ENSG00000178031	19.7603325996576	0.0258744050846556
ENSG00000178568	27.5180140945443	1.07565396326703E-07
ENSG00000178568	24.3478260869565	5.81968691395407E-05
ENSG00000178726	13.8271604938272	0.00489698578846567
ENSG00000178726	12.2430146449565	0.0156330860854684
ENSG00000178796	15.9005323983898	0.0307982983889641
ENSG00000178913	13.6939768148448	0.0350368105979069
ENSG00000178965	14.2696312974951	0.00808516641508364

Table 3 (*continued*)

id	meth.diff	meth.q
ENSG00000179168	17.4945100909756	0.0282001376411957
ENSG00000179636	20.9585643419901	0.0220602019465386
ENSG00000179698	10.7581561220446	0.041618804863787
ENSG00000179698	12.4260355029586	0.000242145115872396
ENSG00000179862	30.6855636123929	0.0340220750692895
ENSG00000179862	31.8367346938776	0.0473541282756217
ENSG00000180035	27.2213855421687	0.00125428492354235
ENSG00000180035	21.2121212121212	2.95009274710322E-05
ENSG00000180035	13.9821235937741	0.00317629723505787
ENSG00000180061	10.306341393051	0.016226004542076
ENSG00000180071	13.3963417501293	0.049540677234967
ENSG00000180535	27.2674953959484	0.0123714822722483
ENSG00000180535	30.4133568696676	3.48980020306252E-05
ENSG00000181867	11.7798103234996	0.018306081939418
ENSG00000182175	18.0971659919028	5.80609091628168E-05
ENSG00000182175	11.1104582843713	0.0199735193033375
ENSG00000182636	15.5402283677645	0.0126531387699157
ENSG00000183145	29.3362193362193	0.00926579917665838
ENSG00000183145	13.9260640631856	0.0192253482887195
ENSG00000183496	11.2032238578196	0.0074459077399667
ENSG00000183496	14.5393689412893	0.000320527649816425
ENSG00000183605	15.0648824006488	0.0303008750130128
ENSG00000183734	16.6808029403449	0.0281162336753472
ENSG00000184005	16.106135986733	0.00865451355324339
ENSG00000184113	15.9938784938785	0.0229272665000222
ENSG00000184408	15.9975819857942	0.000678111680074365
ENSG00000184672	14.7358898326381	0.0435408963672579
ENSG00000184731	13.2576254294631	0.0104233490346365
ENSG00000184922	25.2331606217617	2.42984978950435E-06
ENSG00000185024	19.2857142857143	0.0135154364114851
ENSG00000185278	10.0415503473349	7.16094124589841E-06
ENSG00000185278	11.3561664874827	2.51200912416616E-06
ENSG00000185742	19.151173422737	0.0008552619353144
ENSG00000185742	15.1043660559657	0.00314120109200504
ENSG00000185774	20.952635804121	0.0397044858541228
ENSG00000185813	15.2209951485897	0.0181017550145296
ENSG00000185825	12.8256688232208	5.28646186599738E-05
ENSG00000185825	10.0686749295466	0.0401229285764378
ENSG00000185896	10.5979766173941	0.024117608616727
ENSG00000185896	20.1874052638832	0.024131183824719
ENSG00000185896	13.7539177418424	3.0049488144737E-05
ENSG00000185905	12.3398479913138	0.000156319984376192
ENSG00000185905	14.0702500253062	0.00153387336316091
ENSG00000185958	16.1471861471861	0.0307218007696011
ENSG00000186073	14.7708578143361	0.0174551525895769
ENSG00000186197	19.3347193347193	0.000387011438726581
ENSG00000186523	21.9221835075494	0.0405200413725175
ENSG00000186998	21.6491228070175	0.0107697078177381
ENSG00000187122	12.6247181293053	0.0425111463293409
ENSG00000187135	24.4343891402715	0.0102763374326046
ENSG00000187231	24.3589743589744	0.0244160737034669
ENSG00000187266	15.5664069780445	0.0240826009703214
ENSG00000187527	18.0937892398339	0.00270096155507299
ENSG00000187527	27.905701754386	0.0122003472943511
ENSG00000187821	17.3017586961799	0.0262473787545817
ENSG00000187848	49.1819291819292	3.72008212902467E-10
ENSG00000188153	12.1476617552851	0.0439126087216701
ENSG00000188162	32.9668348954578	0.0274261593096852
ENSG00000188229	11.2701937064543	0.00466411582880679
ENSG00000188493	14.2631246046806	0.0052381158340976
ENSG00000188522	29.9446964518735	0.0024547054883833
ENSG00000188822	19.4871794871795	0.0431051281570937
ENSG00000188916	18.2413204325555	4.63633125090392E-06
ENSG00000196074	12.1661315424197	0.0106092170610959
ENSG00000196074	10.6353071608165	0.00457266157639662
ENSG00000196090	14.2025776415148	0.00695143377982781
ENSG00000196090	14.810846844273	0.0063343819436355
ENSG00000196132	15.3465882437845	0.0118293720940106
ENSG00000196277	19.1864578603335	0.00237980339670023
ENSG00000196358	36.0210777490555	0.000800203526648617
ENSG00000196361	34.7555923777962	0.00223050817172084
ENSG00000196418	37.8125	0.0495930018339292
ENSG00000196498	23.0205156060669	5.350072520849E-05
ENSG00000196570	18.4998443821973	0.022094705739058

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Table 3 (*continued*)

id	meth.diff	meth.q
ENSG00000196576	20.02442002442	0.0143206955470071
ENSG00000197321	26.6782608695652	0.0141433998222048
ENSG00000197355	20.8519179304193	0.000840561887852749
ENSG00000197442	12.9341199606686	0.0468764097793746
ENSG00000197497	13.7522892102181	0.000266565975725615
ENSG00000197620	24.2486554887694	0.00550099733479635
ENSG00000197713	15.7586006447181	0.000195240360198019
ENSG00000197713	12.9293159423592	0.00174790476518585
ENSG00000197977	13.1134277680514	0.00393456326723536
ENSG00000197977	20.7747752921919	2.32967856639697E-05
ENSG00000198055	18.4998443821973	0.022094705739058
ENSG00000198435	12.6049245940254	0.0352599400113216
ENSG00000198538	11.0856852275616	0.034699107985298
ENSG00000198553	12.7099236641221	0.0324911160618064
ENSG00000198553	16.3043478260869	0.00529968603181151
ENSG00000198625	13.7817587098737	6.35144577459527E-05
ENSG00000198691	16.1113699906803	0.0178381603850453
ENSG00000198691	16.1113699906803	0.0178381603850453
ENSG00000203734	18.4851120338159	9.09164293803858E-05
ENSG00000204104	15.3368121442125	0.0219176387353552
ENSG00000204104	15.3368121442125	0.0219176387353552
ENSG00000204231	16.1843515541265	0.0363731258486073
ENSG00000204231	15.0719651642069	0.0222603667551141
ENSG00000204524	16.3571716688827	0.0281033417170994
ENSG00000204538	17.7033492822966	0.0186818574618526
ENSG00000204604	11.0856852275616	0.034699107985298
ENSG00000204612	18.7839937839938	0.00250813598583812
ENSG00000204612	16.5474182682596	0.00148912704912215
ENSG00000204764	45.4649588670207	3.9838278218345E-12
ENSG00000205022	38.382257012394	0.000546765217802043
ENSG00000205358	13.0402817859612	0.0436043261973361
ENSG00000211887	10.8259823576584	0.0293719445323917
ENSG00000211888	10.8259823576584	0.0293719445323917
ENSG00000211904	25.2304811293575	0.0199603966385628
ENSG00000211905	25.2304811293575	0.0199603966385628
ENSG00000211967	29.6948356807512	0.047288778192247
ENSG00000213337	20.1949317738791	0.0481825564972396
ENSG00000213563	20.0679658366414	4.60696397442978E-06
ENSG00000213585	12.0044548440804	2.76132243255278E-07
ENSG00000215131	13.6776422610731	0.0301144898207834
ENSG00000215131	17.3587154236969	0.0164588521031709
ENSG00000215218	62.7596721936345	1.23161776512788E-11
ENSG00000215375	24.7302410313901	0.000291709269699351
ENSG00000215612	25.1071179459926	0.00154876825761241
ENSG00000220201	14.9630274032188	0.00661633019678567
ENSG00000221890	13.7059142702116	0.0467389184859929
ENSG00000221890	22.6050420168067	0.0345626215065825
ENSG00000222014	23.8909634055265	0.0395536522028147
ENSG00000224051	30.1339896089691	0.0291683709558524
ENSG00000224982	11.9933191381297	0.0336814320680362
ENSG00000225528	16.3925127623369	0.0436056297319412
ENSG00000225528	31.4965408423352	0.0162309007913253
ENSG00000226174	19.4751640112465	0.0458245501469545
ENSG00000226807	19.5400013256446	0.000741069205726134
ENSG00000230778	36.6425783514318	1.53623391923156E-06
ENSG00000235007	12.1781869246372	0.000684486983272381
ENSG00000236597	25.2304811293575	0.0199603966385628
ENSG00000237521	11.8684113978232	0.0372737808864645
ENSG00000238205	39.5	0.0123595376844097
ENSG00000240041	25.2304811293575	0.0199603966385628
ENSG00000241878	14.4855688682885	6.15403543233231E-07
ENSG00000242887	25.2304811293575	0.0199603966385628
ENSG00000243811	10.9948112363571	0.012370849740844
ENSG00000243811	20.4896907216495	0.0239166953197774
ENSG00000243910	26.4705882352941	0.0319767800481153
ENSG00000249715	12.6467285903848	0.0355790310664249
ENSG00000250312	40.0960827790096	0.0238001723600601
ENSG00000253873	16.2661776264082	0.00844151005684433
ENSG00000254167	15.7396250735562	0.00428564303869565
ENSG00000254656	25.5557672764228	6.97580628217678E-05
ENSG00000254656	23.0608724225745	0.000886141005522823
ENSG00000255432	18.7762014492351	0.0187775057128133
ENSG00000257950	31.5746753246753	0.00664142162914082
ENSG00000258555	14.238574492658	0.00257404896789635

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Table 3 (*continued*)

id	meth.diff	meth.q
ENSG00000258588	17.0111238971998	2.8674824329256E-05
ENSG00000258588	17.4084595959596	0.000242040623929651
ENSG00000258947	38.1408450704225	0.0406766051931808
ENSG00000258947	48.0519480519481	0.0233247232177374
ENSG00000260903	14.7750399639444	0.00194658086042017
ENSG00000268089	41.6075650118203	0.00169713877307405
ENSG00000269179	27.7445652173913	0.00395963160047802
ENSG00000269556	20.2995867768595	0.0233828766140779
ENSG00000269556	27.2380570052188	0.0271154900160762
ENSG00000270185	51.3157894736842	0.0114374641511294
ENSG00000270647	13.6887306242145	0.0340582253498451
ENSG00000272297	17.3148504684893	0.000716521181689353
ENSG00000272674	18.5499058380414	0.045620588761505
ENSG00000273559	13.2909328114808	0.00698099756874393
ENSG00000274523	10.4329004329004	0.0490673225866567
ENSG00000274997	11.3590263691684	1.80362232316675E-09
ENSG00000275183	21.6338207247298	0.0263061606240809
ENSG00000277494	17.5513524506813	0.0489012910315538
ENSG00000278318	14.3568939512144	0.00278221664468368
ENSG00000278318	11.0946344439549	0.0235804961090268
ENSG00000278615	18.7762014492351	0.0187775057128133
ENSG00000279301	14.9986327590922	0.0358444715341303
ENSG00000283428	14.5281551621609	0.0269976535385308
ENSG00000284479	24.417945690673	0.00156850485441185
ENSG00000284976	24.8106060606061	0.0406005676956223
id	meth.diff	meth.q
ENSG00000003400	-13.0225905823676	0.0261886189599571
ENSG00000005073	-11.4742264489008	0.00408833030390649
ENSG00000005073	-11.3833525260578	0.00652630708889119
ENSG00000005189	-14.1243862520458	0.0117387368539422
ENSG00000005249	-22.4074705782023	0.0352264426559156
ENSG00000005249	-15.4167949096437	0.0091222647432768
ENSG00000008128	-25.3486464315012	0.000465458078818736
ENSG00000010030	-15.5217903415783	0.0407326950579055
ENSG00000011465	-15.7456922162804	0.00476646652256708
ENSG00000011677	-15.3903308896374	0.0355759656096261
ENSG00000013375	-18.7974626999017	0.000142007746958989
ENSG00000013563	-24.0516545601291	0.0292778679893094
ENSG00000022976	-12.6479289940828	0.0252722406682501
ENSG00000023191	-10.4196194039723	0.0179302817320542
ENSG00000029534	-22.2705696202532	0.0154280889548072
ENSG00000035928	-18.6948694869487	0.00661633019678567
ENSG00000037280	-28.6324786324786	0.000113858936619995
ENSG00000037897	-13.2831444200079	0.0266330771143665
ENSG00000040531	-18.9925925925926	0.00373615812375045
ENSG00000040531	-19.751056964842	4.01914267959484E-11
ENSG00000040531	-10.1102852823329	0.005665190996256
ENSG00000041988	-12.7544307716121	0.0079544377861888
ENSG00000047849	-18.2554287817446	0.0121742321252513
ENSG00000053501	-15.0684931506849	0.00762921671917297
ENSG00000054938	-23.3424567997059	6.90248566006469E-07
ENSG00000055955	-30.8197855413352	0.0447552421906043
ENSG00000057468	-11.2298918708992	0.00886470049709088
ENSG00000057468	-11.2298918708992	0.00886470049709088
ENSG00000058335	-28.6184210526316	0.021551196675812
ENSG00000061455	-17.042217042217	0.0395150600972023
ENSG00000061455	-17.8731762065095	0.0291279908353443
ENSG00000063245	-29.8245614035088	0.00238767155978859
ENSG00000064309	-13.5096968555828	0.00274623489394904
ENSG00000064489	-18.0312897671981	7.66402129046302E-11
ENSG00000064489	-11.0689307272696	2.42044046543343E-05
ENSG00000064490	-12.9920364050057	4.69893374366678E-05
ENSG00000064490	-18.0312897671981	7.66402129046302E-11
ENSG00000064490	-11.0689307272696	2.42044046543343E-05
ENSG00000065665	-25.9183673469388	0.0279148217974277
ENSG00000067840	-25.5321766949674	0.0318898662698066
ENSG00000068831	-21.2225274725275	0.0176828752271213
ENSG00000069667	-31.0036671004097	1.45503265323416E-10
ENSG00000069667	-34.0985832454934	3.94666393261877E-09
ENSG00000070526	-12.1204579392733	0.00116892883638087
ENSG00000071054	-15.9047619047619	0.0193214939202338
ENSG00000071054	-14.9546683023135	0.0294939797114423
ENSG00000071246	-20.5575757575758	0.00952758607868016
ENSG00000072736	-11.8219296976711	0.039605780802127
ENSG00000074317	-14.8832515572259	0.00327521117174258

Table 3 (*continued*)

id	meth.diff	meth.q
ENSG00000074527	-17.6912487708948	0.00153326978684318
ENSG00000074527	-29.7578828828829	2.32852552380807E-07
ENSG00000076662	-14.6666666666667	0.0178617418311501
ENSG00000081087	-10.7036870503597	0.024280154447413
ENSG00000085185	-12.9503169855334	0.0012299560929773
ENSG00000085719	-24.3063912831355	0.00523531558745069
ENSG00000087074	-16	0.0109242806066318
ENSG00000087076	-32.8944618599791	0.0373715106173832
ENSG00000087269	-13.5926535562679	0.0214541103864009
ENSG00000087269	-11.5588273279091	0.0292988774562968
ENSG00000088305	-11.6281866281866	0.0427151981393461
ENSG00000089163	-11.6727376062414	0.0380803051192107
ENSG00000089356	-15.3979991300565	0.0389538034184871
ENSG00000090975	-18.4948822296214	0.0320990923624484
ENSG00000090975	-16.8482117513483	0.00248333432253196
ENSG00000090975	-26.3362068965517	0.0330829773524249
ENSG00000091640	-17.1887796887797	0.0391464914463182
ENSG00000092036	-13.8428155282088	0.00590952601630159
ENSG00000092847	-17.1730139751857	0.00350462007914844
ENSG00000099308	-32.6042378673958	0.000411211410265582
ENSG00000099326	-19.1756272401434	0.0433201581859275
ENSG00000100154	-29.8284256897751	0.00023937218706629
ENSG00000100324	-22.0239481899082	0.0065659318113759
ENSG00000100417	-22.0987654320988	0.000320527649816425
ENSG00000100417	-16.4880952380952	0.00798977532106798
ENSG00000100462	-14.8990364474235	0.0382347891822333
ENSG00000100462	-16.7780783436508	0.00287845042103186
ENSG00000100650	-11.8654311039484	0.0326720487121621
ENSG00000100842	-29.4416399901502	4.41221894215986E-11
ENSG00000100842	-33.4745340376757	1.57828678813707E-09
ENSG00000100842	-18.0075840643275	0.0302217013684655
ENSG00000100983	-17.9347968631154	0.00964959585556572
ENSG00000101126	-14.0618841150966	0.00587985622880035
ENSG00000101146	-46.3265306122449	0.00730784583795025
ENSG00000101188	-17.1462829736211	0.025914734875891
ENSG00000101216	-10.3382163724572	0.0370962647151181
ENSG00000101246	-13.2554549434345	0.0464070147864675
ENSG00000101282	-12.6426591470327	0.000122122341510126
ENSG00000101333	-15.386492289674	0.006884029143443
ENSG00000101445	-15.8599476439791	0.00700729207991631
ENSG00000101463	-20.5708661417323	0.0126535233533451
ENSG00000101489	-12.8653907837058	0.00122182854297472
ENSG00000101850	-45.7032411537318	2.79648097865614E-08
ENSG00000102081	-10.752688172043	0.0317139609470535
ENSG00000102387	-19.7678018575851	5.12150640091635E-07
ENSG00000102409	-13.0988450577471	6.69073628060357E-05
ENSG00000102898	-22.1505376344086	0.0253551987953626
ENSG00000102898	-13.7839737582006	0.00814065825509914
ENSG00000103194	-13.7551771744133	0.0375901937391954
ENSG00000103199	-16.4232218449086	0.00130471132303523
ENSG00000103227	-19.5967357469363	0.0493579705524396
ENSG00000103742	-11.8318663094783	0.0312017387759491
ENSG00000104299	-11.8751264926128	0.01769137676129
ENSG00000104818	-16.7496106894336	0.0252435277943326
ENSG00000104969	-24.4159883528555	0.00479288133087388
ENSG00000104976	-29.2960597052685	0.00253837046745113
ENSG00000105063	-17.0643350701044	0.0190330469630085
ENSG00000105193	-17.1887159533074	0.0363822127069507
ENSG00000105229	-18.4522905318895	0.0444289457526795
ENSG00000105270	-23.5294117647059	0.00688536703967539
ENSG00000105278	-23.4672631850641	0.000755438972190894
ENSG00000105370	-37.6114081996435	0.00458280012729838
ENSG00000105516	-21.0976523476523	0.0222779988761963
ENSG00000105550	-27.290780141844	8.5961537559472E-06
ENSG00000105552	-16.6190476190476	0.0166368308688395
ENSG00000105552	-12.2747099004197	0.0213279395522083
ENSG00000105568	-14.599785512333	0.00298145839645139
ENSG00000105609	-25.4920714825069	0.014731951681206
ENSG00000105639	-10.6699490065061	0.00837345213299676
ENSG00000105639	-11.5959821428571	0.00328479040719733
ENSG00000105655	-30.9553938627017	0.0168610619104421
ENSG00000105655	-27.6315789473684	0.000286470074845706
ENSG00000105852	-14.6870554765292	0.0375158059469258
ENSG00000105989	-19.7711245302141	0.00207953564236401
ENSG00000105989	-14.9031811894882	0.0128575818853282

Table 3 (*continued*)

id	meth.diff	meth.q
ENSG00000106144	-12.3389400190416	0.0314189626104258
ENSG00000106244	-14.7058823529412	6.15633218377445E-05
ENSG00000106245	-14.7058823529412	6.15633218377445E-05
ENSG00000107282	-12.6867335562988	0.0337841907588973
ENSG00000107362	-11.3020890206718	0.015856947109812
ENSG00000107443	-20.8430295324233	2.10698806649647E-05
ENSG00000107736	-15.539071680376	0.00666888599889314
ENSG00000108381	-20.3422053231939	0.00257135725773325
ENSG00000108839	-13.7001793301776	0.0363397921517671
ENSG00000108984	-17.3495320151243	0.0346550934924646
ENSG00000109458	-12.616004666702	0.0411833707244456
ENSG00000109475	-29.4538606403013	0.0381811229547991
ENSG00000109475	-18.9792663476874	0.0451290699962029
ENSG00000109738	-35.099846390169	0.0327601799288268
ENSG00000110148	-33.2332933173269	0.00346896135886557
ENSG00000110660	-21.9194342095502	0.000235854083096956
ENSG00000110900	-14.5840229504579	0.0299976369432143
ENSG00000110975	-20.0274364785876	0.00272717077717902
ENSG00000111664	-15.6848179488836	0.00257413439830448
ENSG00000112309	-30.8820662768031	2.86639765886729E-06
ENSG00000112541	-18.4981562185719	0.0200177787462048
ENSG00000112576	-16.3205266840532	0.00281098485768811
ENSG00000113356	-30.4485219164118	0.0128237638132768
ENSG00000113356	-30.4485219164118	0.0128237638132768
ENSG00000113360	-13.2024460073839	0.000889075765212803
ENSG00000113360	-11.4206595619703	0.0395953589414958
ENSG00000113396	-10.7508473103328	0.000222229285000517
ENSG00000113719	-40.4600301659125	0.00364018917025852
ENSG00000114391	-14.7478070175439	0.000179247076510977
ENSG00000114391	-14.5098841172461	0.000278596416985043
ENSG00000114473	-12.5049648435403	0.00644783960827106
ENSG00000114487	-16.8965253036049	0.00508044584013533
ENSG00000114487	-20.4324228659076	0.00210512320114037
ENSG00000114742	-23.7758620689655	0.00189481574489691
ENSG00000114742	-21.9666048237477	0.00854398233095821
ENSG00000114784	-36.394156610108	3.79465602442319E-05
ENSG00000115539	-10.9105125366788	0.0163551846730581
ENSG00000115616	-12.828429432203	0.0317264087153831
ENSG00000115761	-15.6470588235294	1.34064823464507E-05
ENSG00000116014	-18.3325135268077	0.0328810899473227
ENSG00000116017	-24.6754643907337	0.00721459066489451
ENSG00000116497	-15.2564510990761	0.0325259241056017
ENSG00000116497	-11.8800281184097	0.0239625938500126
ENSG00000116580	-15.6574072798887	0.0388050857433615
ENSG00000116815	-15.8136401282222	0.000915128561518491
ENSG00000116962	-15.572105619499	0.0330821942950349
ENSG00000117632	-22.127940529173	0.00508881441496338
ENSG00000117751	-55.1142005958292	0.00823190880858581
ENSG00000118985	-15.2974664454833	0.0372468840756965
ENSG00000119541	-15.2993348115299	0.0255955821057175
ENSG00000119559	-41.9905956112853	0.00238126889066042
ENSG00000119630	-12.5075895567699	0.0450264295667423
ENSG00000119630	-10.7784431137725	0.00695950565232784
ENSG00000119878	-10.8361336915488	0.00655953508969455
ENSG00000119878	-10.9735694413114	0.00835818942302695
ENSG00000120784	-10.4694508425264	0.0102714888088208
ENSG00000121274	-10.2296314811394	0.0408612226104307
ENSG00000121316	-15.976285802279	0.0306290082498898
ENSG00000121316	-16.9739750803858	0.00365812101598888
ENSG00000121316	-13.1297947335683	0.0234652036229857
ENSG00000121690	-24.4730918764068	0.000156981828754297
ENSG00000122691	-14.2683562492956	0.000251244013240575
ENSG00000122863	-17.6983287497356	0.00205605071100639
ENSG00000123130	-37.3015873015873	5.00924521270897E-06
ENSG00000123143	-23.00803673938	0.0478792095442045
ENSG00000123159	-20.3386330786702	0.0177393022391982
ENSG00000123178	-14.8057128610607	0.0275489351598191
ENSG00000123360	-15.4106531766106	0.00851060967044734
ENSG00000123407	-10.9556347791642	0.0142153062123272
ENSG00000124222	-12.3358585858586	0.00423793375162113
ENSG00000124614	-10.6719405397908	0.04406634342951
ENSG00000125207	-23.0804597701149	1.12993284829733E-05
ENSG00000125375	-11.9933456946298	0.0395889380296399
ENSG00000125484	-10.9840042359837	0.00307962939304754

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Table 3 (*continued*)

id	meth.diff	meth.q
ENSG00000125510	-25	0.0405222568610454
ENSG00000125703	-15.0007463800567	0.0266746959628891
ENSG00000125787	-12.9496402877698	0.00114656647454784
ENSG00000125787	-19.3181818181818	0.00173392732935099
ENSG00000125820	-11.3668021986296	0.00382045804138979
ENSG00000126391	-22.9202037351443	0.000154722264355363
ENSG00000126562	-31.8491609335819	2.09007355450092E-05
ENSG00000126870	-15.622650240037	0.0286387794400106
ENSG00000126882	-11.474980351061	0.0431523638296012
ENSG00000127125	-17.3795119886894	0.0283863465926657
ENSG00000127415	-36.1538461538462	0.000655153273081841
ENSG00000127529	-26.0351966873706	0.0223192198423381
ENSG00000127586	-23.5960889504197	0.0106052756412346
ENSG00000127663	-33.3638743455497	0.000100926955366392
ENSG00000127990	-32.3784722222222	0.00950903648521135
ENSG00000128011	-20.6728860658992	0.00861580075079421
ENSG00000128016	-18.5567010309278	0.013230362760599
ENSG00000128016	-18.6214217731898	0.0353039817458317
ENSG00000128298	-20.8948991391494	0.0175681937283948
ENSG00000128422	-13.7385720060132	0.0117581512531377
ENSG00000129472	-21.1173943261515	0.000387158567669044
ENSG00000129484	-10.2674847144049	5.0998273735677E-05
ENSG00000129654	-10.6407004024644	6.26010353840451E-06
ENSG00000129654	-20.2244563946692	6.16199680477102E-11
ENSG00000129654	-13.5787172011662	0.00135771137135729
ENSG00000130045	-12.9216699638587	0.00155013269955672
ENSG00000130045	-15.3130946203079	0.0218319135747878
ENSG00000130159	-18.7433778342869	0.0410766095470683
ENSG00000130182	-13.5927280789269	0.045902210404969
ENSG00000130294	-18.8954248366013	0.00877421386783813
ENSG00000130294	-28.8836229594523	7.24042379336115E-05
ENSG00000130487	-15.3873507747016	0.000529655572901532
ENSG00000130538	-42.8571428571429	0.00933674892573389
ENSG00000130714	-14.0240632969332	0.00963961443844441
ENSG00000130717	-11.0306725090493	0.0150416028353088
ENSG00000130720	-19.3835242771413	0.0472934196741187
ENSG00000131015	-17.3019350127784	0.0489828462430321
ENSG00000131381	-24.6941896024465	0.0275157239159661
ENSG00000131398	-35.6111111111111	0.0356514356017021
ENSG00000131409	-38.4105960264901	0.0015304011826433
ENSG00000131620	-23.3758708893317	7.69815899489769E-05
ENSG00000132199	-12.1509735929581	0.00665502017260467
ENSG00000132773	-18.0035650623886	0.00122867731832998
ENSG00000133111	-21.1876681150424	0.0249387687490626
ENSG00000133243	-11.1267839362761	0.00243882056963042
ENSG00000133321	-13.4793202549044	0.0211467246998243
ENSG00000133321	-16.0883591014595	2.83828725507107E-05
ENSG00000133393	-10.355408388521	0.00435617482647642
ENSG00000133937	-15.1024651024651	0.00679486399082597
ENSG00000133937	-15.7077476299444	0.0373418607525007
ENSG00000133943	-15.2855105139649	0.00238509340205644
ENSG00000133958	-17.9266379142823	5.11406800358734E-06
ENSG00000133958	-29.7367668097282	1.08787851078348E-08
ENSG00000133958	-23.9583333333333	0.0470977877712396
ENSG00000133983	-25.126213592233	0.0333275081725526
ENSG00000134160	-21.6216216216216	0.0311442667394412
ENSG00000134215	-16.6288096607246	0.000979592583486402
ENSG00000134259	-19.9652777777778	0.00459426665426082
ENSG00000134686	-16.0714285714286	0.0353876886095324
ENSG00000135070	-30.6306306306306	0.0287505845364152
ENSG00000135070	-29.2885375494071	0.0148111641287168
ENSG00000135116	-13.5057471264368	0.034558826714043
ENSG00000135116	-13.0969049373618	0.0166690647998171
ENSG00000135452	-15.9663763909047	0.0364290421425044
ENSG00000135625	-13.1926672653561	0.000180728729306327
ENSG00000135747	-14.5836288835296	0.00349485787643516
ENSG00000135747	-13.4898365882822	0.0171288842575121
ENSG00000135776	-10.0856722215261	0.0439649286170108
ENSG00000135821	-16.3918557262899	0.000488928158744758
ENSG00000135821	-18.4593133896628	0.00119169070034406
ENSG00000135824	-12.9420579420579	0.0118868224955648
ENSG00000135968	-24.1077441077441	0.019223536336163
ENSG00000136146	-30.6409130816506	0.0269348481620303
ENSG00000136327	-32.3391812865497	0.00880486435194367

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Table 3 (*continued*)

id	meth.diff	meth.q
ENSG00000136352	-13.5327327327327	0.0236714264555738
ENSG00000136485	-11.0469225080122	0.0100108377098408
ENSG00000136630	-15.0338171894158	0.0403037861767516
ENSG00000136861	-12.3891937526382	0.00589132460144071
ENSG00000137094	-22.8049057460822	3.40669087085994E-05
ENSG00000137094	-13.0273229458248	0.0325217962410283
ENSG00000137198	-28.0144806460596	0.000313980355193008
ENSG00000138131	-15.5605381165919	0.025521439514233
ENSG00000138134	-20.9755709397629	0.0408173872099301
ENSG00000138600	-10.1742758959254	0.0348499608751473
ENSG00000138834	-10.4375895004986	0.0167826181251203
ENSG00000138835	-13.2712583869643	0.0392329312376509
ENSG00000138944	-37.8117457763475	0.0169445660029793
ENSG00000139192	-13.983892321271	0.00885711294205875
ENSG00000139192	-11.6258525762183	0.00751529202601257
ENSG00000139714	-11.1285362853629	0.00582711461235512
ENSG00000139899	-15.5924528301887	0.00708357967547035
ENSG00000140015	-13.9915288422751	0.0428923094078256
ENSG00000140044	-19.5838163051278	0.000727341401953011
ENSG00000140104	-13.5344543356413	0.0289879131876795
ENSG00000140416	-23.959373959374	4.21840608750738E-05
ENSG00000140416	-20.4453441295547	0.0138015923316579
ENSG00000140451	-18.4220251293422	0.0260071904102253
ENSG00000140474	-23.1256085686465	0.0425453638576046
ENSG00000141337	-13.456108559147	0.000382942170809787
ENSG00000141391	-13.0301243304339	0.00610268151373784
ENSG00000141867	-25.8426966292135	0.00119747111310554
ENSG00000141873	-19.2689677629437	0.0139942362377622
ENSG00000141905	-35.3565571954084	6.5431611235357E-09
ENSG00000141905	-27.0154620640058	0.00212688984984319
ENSG00000142273	-19.4395149364094	0.0341414149043605
ENSG00000142507	-11.1580362944047	0.0418281146152015
ENSG00000142621	-45.6707317073171	0.000863683454995586
ENSG00000142731	-21.0726198609492	0.000484552422247172
ENSG00000142867	-13.1578947368421	0.00619428006528507
ENSG00000142867	-13.1578947368421	0.00619428006528507
ENSG00000143033	-18.3116883116883	0.0284952940005011
ENSG00000143033	-18.3116883116883	0.0284952940005011
ENSG00000143355	-12.3834498834499	0.0346025307894399
ENSG00000143374	-15.6125484033896	0.0155077808974864
ENSG00000143374	-17.1239876794688	0.00428702673106584
ENSG00000143379	-13.626623811437	0.00440828768941389
ENSG00000143479	-13.636249655207	0.0401229285764378
ENSG00000143761	-18.0174498055293	0.00381098926362394
ENSG00000143761	-22.6227795193312	0.0255923303695082
ENSG00000143867	-15.8305140941493	7.6395234090418E-06
ENSG00000143921	-13.8744216787839	0.0186267917434666
ENSG00000144229	-22.6389063087922	0.034404389349106
ENSG00000144909	-16.7247386759582	0.00327712188231578
ENSG00000145029	-10.7424071991001	0.0174515769503486
ENSG00000145214	-36.1538461538462	0.000655153273081841
ENSG00000145730	-20.8618331053352	0.0486535583651227
ENSG00000145734	-14.2168981776475	0.0331361591998198
ENSG00000146197	-11.3651300952356	0.0309216170969307
ENSG00000146250	-21.2040252916555	0.00848045384869553
ENSG00000146250	-22.0065591325882	0.00296624203140471
ENSG00000146374	-15.4091075682609	0.00783375990203119
ENSG00000146374	-20.1172319599363	0.0115010741507591
ENSG00000146374	-38.2486388384755	1.37237832032523E-05
ENSG00000147246	-20.514950166113	0.0239095391739468
ENSG00000147251	-26.3721552878179	0.000932126740918554
ENSG00000147394	-11.4991684485626	0.0297789394824325
ENSG00000147548	-13.7248594580519	0.00616478390735392
ENSG00000147548	-13.040664654268	0.0288179691676682
ENSG00000148655	-15.4956427015251	0.00901490620617616
ENSG00000149328	-14.6648803730994	0.0012525258652476
ENSG00000149328	-19.1528624152433	0.00214493242740375
ENSG00000149451	-14.8878885783086	0.0162992720438351
ENSG00000149582	-14.3974688825534	0.0247275946396006
ENSG00000149582	-14.0256827368629	0.000459350694151369
ENSG00000149654	-15.4766951290902	0.015362223159322
ENSG00000149654	-20.1642804175461	0.000992524624161035
ENSG00000151229	-13.166266050701	0.00173813692311102
ENSG00000151725	-15.0714229652304	0.0395704516303525
ENSG00000152193	-15.2238805970149	0.0308984735161578

Table 3 (*continued*)

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ENSG00000152380	-23.051948051948	0.0348877300166107
ENSG00000152700	-29.6397151235861	0.0440101312546697
ENSG00000152977	-22.3263027295285	0.0148703640447006
ENSG00000153201	-25.95867173846	6.03476649807237E-07
ENSG00000153495	-18.1541313559322	0.0412507118962655
ENSG00000153786	-12.0300751879699	0.0146452802851786
ENSG00000153975	-17.2638259994582	0.00550962296253264
ENSG00000154380	-10.5780632411067	0.00338062852938879
ENSG00000154485	-22.2101692240937	0.00385139279194034
ENSG00000154957	-10.5852304975721	0.0272186139291782
ENSG00000154957	-11.9181175784949	0.0231333663975567
ENSG00000156017	-13.5395109245756	0.0214605900398261
ENSG00000156398	-13.6112071947423	0.0442108996079291
ENSG00000157193	-10.0792079207921	0.00307962939304754
ENSG00000158553	-16.7250599299281	1.01677867799016E-06
ENSG00000158850	-16.0014655212734	0.00265513690925244
ENSG00000159086	-48.6111111111111	0.00341946937420944
ENSG00000159111	-15.317317888898	0.0290015907298838
ENSG00000159217	-21.919589706017	4.65076018775794E-13
ENSG00000159217	-21.8456181679169	6.08350558115787E-14
ENSG00000159217	-13.1358159469513	0.00272604922768381
ENSG00000159217	-17.1470999301188	0.00963809575114907
ENSG00000159217	-29.0376091029566	9.73097876752809E-21
ENSG00000159217	-28.7603305785124	5.92217776925561E-12
ENSG00000159409	-15.4835847382431	0.0188191907781351
ENSG00000159592	-30.1703163017032	4.96306823337162E-05
ENSG00000159592	-21.9911969517803	0.00012860799914889
ENSG00000159873	-23.3333333333333	0.0427919778007068
ENSG00000160284	-10.0910730522142	0.00355482199628395
ENSG00000160789	-23.2076407839246	0.0205853009889123
ENSG00000160951	-14.4109149277689	0.038467462223309
ENSG00000160959	-23.3835005574136	0.00101322585276091
ENSG00000161677	-23.7462537462537	0.0236354015373858
ENSG00000161681	-31.2189740761169	0.0241663529211224
ENSG00000161914	-42.1052631578947	0.00358926842407119
ENSG00000162194	-26.884236453202	1.99755793333376E-06
ENSG00000162374	-15.7203751065644	0.0214515366994642
ENSG00000162510	-34.2105263157895	0.0341490515681589
ENSG00000162526	-11.6745825034472	0.022486348070365
ENSG00000162572	-14.9247403010388	0.0205495188120766
ENSG00000162576	-23.2708528584817	0.0018469989151733
ENSG00000162598	-13.216585768218	0.029516186368158
ENSG00000162738	-23.0551626591231	0.0445079711706162
ENSG00000163216	-29.9435028248588	0.0254715229528836
ENSG00000163354	-10.1694915254237	0.00590858951859975
ENSG00000163354	-10.5489734343955	0.0267551521436017
ENSG00000163357	-10.1694915254237	0.00590858951859975
ENSG00000163508	-16.0858149906488	0.041677504344468
ENSG00000163565	-11.0395892164983	0.00942619045704688
ENSG00000163565	-16.6825901668196	5.06081383180988E-06
ENSG00000163792	-16.4178297089689	0.0456416556009675
ENSG00000163935	-28.2106782106782	0.0451608969415679
ENSG00000164008	-15.6722709914199	0.025593910912043
ENSG00000164049	-21.8555093555094	0.0348123187776853
ENSG00000164253	-12.1276434472826	0.0140062768426212
ENSG00000164576	-10.2767967431584	0.00185764298357138
ENSG00000164808	-24.6117882785106	0.00106320574342346
ENSG00000164808	-14.6056693797362	0.0088680500066369
ENSG00000164853	-10.6209444844989	0.0440954421453351
ENSG00000164898	-20.2627939142462	0.00811583720494599
ENSG00000165030	-12.2485195433424	0.00382368928474016
ENSG00000165169	-54.8235294117647	0.0246917998898834
ENSG00000165181	-13.645390070922	0.0108554690065924
ENSG00000165181	-15.7554434688752	1.17460044209381E-05
ENSG00000165181	-11.5519875424874	0.00246095170022225
ENSG00000165194	-15.5302183471198	0.0210567244935989
ENSG00000165572	-10.0391913480215	0.00368247816992669
ENSG00000165626	-18.5858585858586	0.0197444308039569
ENSG00000165626	-10.4583151462244	0.0343280241839522
ENSG00000165688	-12.2080440996325	1.88001695122534E-05
ENSG00000165714	-11.8648473034438	0.00183779313657834
ENSG00000165716	-15.6248478652451	0.0196132833917005
ENSG00000165731	-12.1427535180618	0.0180091631493048
ENSG00000165775	-12.0743034055728	3.59947718491836E-06
ENSG00000165775	-15.0654403961797	9.86078794046642E-09

Table 3 (*continued*)

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ENSG00000165799	-24.1837299391256	0.00857990103345192
ENSG00000165799	-19.8527720266851	0.0447136844752293
ENSG00000165801	-24.4671912000611	0.000480223775456203
ENSG00000165959	-26.508875739645	0.0066475031340021
ENSG00000165973	-20.0363825363825	0.0165481327387899
ENSG00000165985	-30.5448408871745	1.2732236675273E-08
ENSG00000166091	-19.7257850508625	0.027040457578079
ENSG00000166173	-13.8671875	0.00281660749850881
ENSG00000166173	-14.943388164922	0.000592748819450959
ENSG00000166377	-15.276467878841	6.07950471947656E-06
ENSG00000166426	-22.4036511156187	0.0437852700044924
ENSG00000166592	-15.2411982984886	0.0135579700736489
ENSG00000166592	-25.5485893416928	0.0100758731655927
ENSG00000166803	-20.5533596837945	0.00278344805297171
ENSG00000166803	-18.065229408513	0.00528917522230573
ENSG00000166847	-26.7138142385667	0.0319767800481153
ENSG00000166896	-12.7930294300401	0.00190635401196762
ENSG00000167074	-21.9168717528028	0.00476822611347794
ENSG00000167081	-11.5329115329115	0.0192254916025242
ENSG00000167470	-10.062893081761	0.0449721395775338
ENSG00000167476	-38.25	0.0195079520010307
ENSG00000167513	-18.2418326468431	0.00513538343420379
ENSG00000167523	-16.751269035533	5.8315626359607E-08
ENSG00000167523	-17.4025110168787	2.59983673643989E-05
ENSG00000167526	-11.1692867520976	0.00118618030478542
ENSG00000167634	-16.58892394933	0.0196502517532655
ENSG00000167671	-12.8785228377065	0.013573497275049
ENSG00000167851	-10.7694353573233	0.00869527291826573
ENSG00000167851	-12.1889157822876	0.0117343371568843
ENSG00000167881	-26.2898150453897	0.000434071699893402
ENSG00000167996	-10.9699648123324	0.0187914208163955
ENSG00000168038	-22.1369316957552	0.00724974359040535
ENSG00000168038	-25	0.00266342702191425
ENSG00000168175	-10.1085977789299	2.69470160653853E-06
ENSG00000168175	-13.507607398568	9.77047420209518E-06
ENSG00000168269	-25.6733573511752	1.75027828135518E-09
ENSG00000168269	-10.7177100894752	0.0055792105653023
ENSG00000168269	-18.1694737322562	0.00716701190068403
ENSG00000168303	-10.4314805239289	0.000306902994481113
ENSG00000169057	-19.6876932591218	0.026724249858753
ENSG00000169083	-23.5576923076923	0.0187144195458153
ENSG00000169084	-29.0322580645161	0.00483664148292746
ENSG00000169093	-31.3492063492063	0.0365158697709021
ENSG00000169100	-28.75	0.0250757960225838
ENSG00000169230	-22.6702952333828	0.0422632036507693
ENSG00000169242	-15.2898949137421	0.00804460478387819
ENSG00000169439	-14.8148148148148	0.0348352182574728
ENSG00000169609	-24.4485294117647	0.00825846345734721
ENSG00000170421	-11.9796380090498	0.0442678426582623
ENSG00000170906	-17.3944093042236	0.00018791758917765
ENSG00000170961	-23.5421686746988	0.00034629022757534
ENSG00000170961	-10.357760079819	0.000129085578271494
ENSG00000171357	-26.2054681027341	0.00139141019560311
ENSG00000171448	-10.0970016329942	0.0272909112444354
ENSG00000171490	-10.0909620468701	0.0304261330467838
ENSG00000171540	-16.0863742885839	0.0218407491899384
ENSG00000171540	-16.5043695380774	0.0490076716034
ENSG00000171695	-18.0929778025967	8.69053858390073E-05
ENSG00000171695	-20.9542066027689	0.0020914999076222
ENSG00000171777	-16.0386774797255	0.000440982847656926
ENSG00000171811	-16.2222724362596	0.0150934255049598
ENSG00000171811	-19.6726772550452	0.00308927350924729
ENSG00000171824	-12.1212121212121	0.0220298071571259
ENSG00000171827	-20.2595729013255	0.00112689504985543
ENSG00000171827	-10.5717191529549	0.0405200413725175
ENSG00000171885	-21.1733080328906	0.0300082453887271
ENSG00000172009	-24.4159883528555	0.00479288133087388
ENSG00000172175	-24.6776273372018	0.0251899708065854
ENSG00000172175	-32.8273244781784	0.016068778755576
ENSG00000172175	-13.6658199347632	0.0450575089860559
ENSG00000172175	-18.6102466574458	0.012763378554628
ENSG00000172183	-14.7980689979983	0.00039915484149278
ENSG00000172201	-11.4285714285714	0.042727357222922
ENSG00000172247	-24.1772860943845	0.000756263656187047
ENSG00000172247	-22.1130952380952	0.0151972472985044

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Table 3 (*continued*)

id	meth.diff	meth.q
ENSG00000172543	-17.4823053589484	0.0217420827203701
ENSG00000172977	-15.757705479452	0.0330323736724333
ENSG00000173530	-16.4157644250816	0.0412017199604227
ENSG00000173535	-23.287380699894	0.0342494992145822
ENSG00000173572	-19.6588967145891	3.55848863666085E-06
ENSG00000173572	-16.3610193887055	0.0037142313706764
ENSG00000173838	-10.265975242556	0.0440156989220841
ENSG00000173926	-37.8290903821071	1.03898737983963E-08
ENSG00000174125	-14.4927536231884	0.0224341959055047
ENSG00000174130	-14.4927536231884	0.0224341959055047
ENSG00000174238	-19.4229028637631	0.000501109262746203
ENSG00000174358	-18.1610431509612	0.0369536902924354
ENSG00000174460	-13.1848284166165	0.0180513136022626
ENSG00000174527	-18.6987248716345	0.0295172703754136
ENSG00000174586	-16.0897801884099	0.0232162403378778
ENSG00000174611	-10.2596396047278	0.000836643340794033
ENSG00000174917	-27.7447219789181	7.86270040653903E-05
ENSG00000175175	-17.5662061024755	0.00310539182240812
ENSG00000175175	-13.876012145749	0.0223192198423381
ENSG00000175938	-19.1143728869465	0.000609551618847887
ENSG00000176720	-15.028624757978	0.000491904426861521
ENSG00000176720	-18.056002574831	0.000841690120167665
ENSG00000176973	-27.5773195876289	0.0385986893303241
ENSG00000177042	-12.1807497077709	0.00600774773082857
ENSG00000177106	-16.1576011157601	0.0274773889313824
ENSG00000177106	-12.1807497077709	0.00600774773082857
ENSG00000177674	-18.691169878978	0.0283655568248335
ENSG00000177992	-10.8843537414966	0.0114479177109907
ENSG00000178201	-13.7678872053872	0.0129363494631834
ENSG00000178209	-12.8916281458654	0.0224823455081024
ENSG00000178234	-18.9923469387755	0.0193669089939285
ENSG00000178234	-22.2923816060398	9.30459330102401E-05
ENSG00000178645	-12.648988053376	0.0469137584786117
ENSG00000179094	-13.4310850439883	0.0355759656096261
ENSG00000179331	-21.9194342095502	0.000235854083096956
ENSG00000180287	-24.0886330665918	0.00852227254789977
ENSG00000180818	-11.8653524270039	0.0285551186534443
ENSG00000180834	-18.060221475675	0.0201026712084086
ENSG00000181104	-13.6891228909896	0.0435232730481889
ENSG00000181104	-18.0640976638058	1.14813876834968E-05
ENSG00000181104	-22.6280986455405	0.000111828657367155
ENSG00000181192	-12.6157900070944	0.00754488631590946
ENSG00000181350	-18.2209259934378	0.000396760300992857
ENSG00000181392	-13.9805515702216	0.000969860854511591
ENSG00000182111	-10.9364529819075	0.012680610291506
ENSG00000182149	-35.0862068965517	0.00826722019021418
ENSG00000182256	-16.1525907792738	0.038574221482599
ENSG00000182348	-18.1128025756191	0.0194939041437827
ENSG00000182508	-13.0498281786942	0.032867434303606
ENSG00000182508	-14.4618262692722	0.00166153295956751
ENSG00000182687	-26.2898150453897	0.000434071699893402
ENSG00000183048	-18.5163996948894	0.0208771553597651
ENSG00000183715	-10.8016877637131	0.00612124554796258
ENSG00000183733	-10.0493848806289	0.00256565663957455
ENSG00000183837	-30.594441063096	0.00594580436285597
ENSG00000183837	-28.5073037127206	5.99242522804126E-05
ENSG00000184209	-19.0350877192982	0.00357549061671981
ENSG00000184209	-14.5669093648004	0.0101738819058995
ENSG00000184220	-10.7100415923945	0.0189969303520165
ENSG00000184226	-20.1388888888889	0.00122241909616555
ENSG00000184254	-14.297763338748	0.0098100477552559
ENSG00000184445	-28.9085545722714	1.10468522189305E-19
ENSG00000184470	-10.5525364848336	1.22641272400171E-07
ENSG00000184486	-11.9779353821907	0.0197742056775144
ENSG00000184486	-14.6947506993582	0.0308993694062091
ENSG00000184903	-17.3484848484848	0.0100846794029084
ENSG00000185085	-12.7741935483871	0.00355548903022132
ENSG00000185164	-28.9317134478425	0.00766039313216227
ENSG00000185198	-20.9677419354839	0.00800363463509878
ENSG00000185274	-36.7777777777778	4.13866236096393E-08
ENSG00000185551	-25	4.12989508384209E-05
ENSG00000186094	-15.7203751065644	0.0214515366994642
ENSG00000186994	-17.9708162334701	0.0380436486008334
ENSG00000187049	-21.4250497288291	0.000190407930326322
ENSG00000187094	-30.3257394084732	0.0148136929111902

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Table 3 (*continued*)

id	meth.diff	meth.q
ENSG00000187773	-24.3055555555556	0.010424771548779
ENSG00000187800	-18.8722605235133	0.00097347513700514
ENSG00000188051	-13.5283993115318	0.0284862998415288
ENSG00000188051	-16.4764492753623	0.00830673370301929
ENSG00000188177	-24.021164021164	0.00403947268078688
ENSG00000188389	-18.1108669779365	0.00597294639909556
ENSG00000188501	-16.9491525423729	0.0264267102325099
ENSG00000188529	-15.3846153846154	0.0488977801585413
ENSG00000188554	-16.2792058516196	2.78883070497941E-05
ENSG00000188706	-10.5804820799856	0.0407427459034703
ENSG00000188706	-18.876314577561	0.000205941242025698
ENSG00000188807	-14.1644210192597	0.00214158534118136
ENSG00000188921	-16.1585066317341	0.0076260149012931
ENSG00000188921	-17.3934430588423	0.00829600867835282
ENSG00000188981	-10.4969898808761	0.0245604522604636
ENSG00000189099	-10.7433380084151	0.0471893075050864
ENSG00000189120	-26.8765133171913	0.0118293720940106
ENSG00000189120	-16.2003903708523	0.0123035857744294
ENSG00000189134	-21.6028708133971	0.0420091386650367
ENSG00000196110	-13.8728706833698	0.0420544804809331
ENSG00000196123	-11.8119658119658	0.0011790794908365
ENSG00000196381	-10.4694508425264	0.0102714888088208
ENSG00000196407	-16.2735824568326	1.63439555606411E-10
ENSG00000196407	-16.9854280510018	3.65742313994721E-10
ENSG00000196440	-21.7175066312997	0.0141480507556097
ENSG00000196460	-12.2420683467906	9.84035291008814E-05
ENSG00000196636	-15.222285848148	0.0128524806273957
ENSG00000196653	-28.7365177195686	0.000498526638073357
ENSG00000196923	-10.1846285959639	0.0125269750370792
ENSG00000197079	-15.5820105820106	0.0385511399220718
ENSG00000197081	-21.8181818181818	0.00318594967466865
ENSG00000197128	-17.6767676767677	0.0134216004209188
ENSG00000197128	-20.2912102591504	0.0247558735443318
ENSG00000197451	-11.3869559539578	0.00256448161697349
ENSG00000197451	-21.9268510258698	1.00569142011319E-07
ENSG00000197557	-28.8865979381443	0.0260989117867014
ENSG00000197766	-27.8711484593837	0.0367699367462675
ENSG00000197785	-15.5625079271128	0.0058251957156053
ENSG00000197935	-21.5945242456377	0.000214694174478014
ENSG00000197991	-15.5700753252682	0.0450051741900873
ENSG00000198125	-10.6796116504854	0.041804252368166
ENSG00000198125	-10.6796116504854	0.041804252368166
ENSG00000198171	-11.3691260430391	0.0492812514169258
ENSG00000198208	-12.0056651051313	0.0134097078395219
ENSG00000198231	-10.7800751879699	0.0425875740986927
ENSG00000198464	-16.8132902878666	0.0230462164545817
ENSG00000198561	-10.5533596837945	0.00500520808218314
ENSG00000198633	-12.5153938057164	0.0405828566192806
ENSG00000198729	-15.178272046496	0.00629617981725982
ENSG00000198797	-14.8354404976921	0.00662519298755446
ENSG00000198885	-24.6820349761526	0.025466515731314
ENSG00000198911	-10.7121944078466	0.00210231479703907
ENSG00000198944	-15.3587625526401	0.0293127616163585
ENSG00000203883	-12.3390634262004	0.0146275199407374
ENSG00000204128	-24.5085483767689	0.0052252260379734
ENSG00000204128	-33.2793334876186	9.50251948882142E-06
ENSG00000204161	-18.4558131926553	0.0110080534024279
ENSG00000204161	-16.8376205787781	0.0451923472289257
ENSG00000204308	-18.1073374959397	0.0218284313380497
ENSG00000204308	-19.8579431772709	0.0166281458453145
ENSG00000204397	-25.547055684042	0.036555069792132
ENSG00000204599	-22.2016522344979	0.00142926075835363
ENSG00000204599	-15.4369398207426	0.0188931632771714
ENSG00000204704	-14.9842086793777	0.0295866997565394
ENSG00000204704	-14.9842086793777	0.0295866997565394
ENSG00000204889	-13.903743315508	4.01874758669504E-05
ENSG00000204909	-10.4985439596305	0.000245160528169384
ENSG00000204920	-10.3541162486425	0.0375594462005039
ENSG00000205221	-10.2626190688151	0.0166542415969332
ENSG00000205364	-14.3932579717191	0.0209663026917388
ENSG00000205364	-22.7849311575727	2.75613743411553E-08
ENSG00000205544	-25.2622377622378	0.0374908539061022
ENSG00000205659	-20.3245942571785	0.00640464663479342
ENSG00000205659	-17.2039116262224	0.00192938109327571
ENSG00000205702	-31.1950970377937	0.00353438535321241

Table 3 (*continued*)

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ENSG00000205702	-30.6146572104019	0.00836764608199518
ENSG00000205730	-16.9912609238452	0.00548780640878567
ENSG00000206172	-17.1837108213224	0.00285232058509603
ENSG00000206262	-12.5686982199984	0.0372534055870424
ENSG00000206262	-13.4922856787358	0.0125498653646383
ENSG00000211644	-10.7890102148644	0.00621622387146682
ENSG00000211647	-22.3450830713965	0.0119776508408652
ENSG00000212747	-17.5645161290323	0.034797418404917
ENSG00000213463	-25.126213592233	0.0333275081725526
ENSG00000213999	-18.0312897671981	7.66402129046302E-11
ENSG00000213999	-11.0689307272696	2.42044046543343E-05
ENSG00000214212	-20.3813785733369	0.00225671200629606
ENSG00000214891	-13.9580680757151	0.0388767095822126
ENSG00000215217	-25.9943714821764	3.04217072748092E-05
ENSG00000215472	-27.8483245149912	0.0397619153720593
ENSG00000215817	-13.5190841590305	0.00675659074205503
ENSG00000217236	-20.5956813104989	0.0287502245020191
ENSG00000221988	-15.437030075188	0.000881217599989722
ENSG00000221988	-12.5576953684546	0.0151972472985044
ENSG00000223547	-41.025641025641	0.048531701906358
ENSG00000223547	-41.025641025641	0.048531701906358
ENSG00000223547	-36.1852433281005	0.00120676448013167
ENSG00000224041	-26.5662172878668	0.0141737948892525
ENSG00000224470	-35.0862068965517	0.00826722019021418
ENSG00000232237	-18.4426964277711	0.00706947340347165
ENSG00000232434	-15.4621775059731	6.92750811815583E-05
ENSG00000233041	-25	0.0498242721317406
ENSG00000233436	-10.5533596837945	0.00500520808218314
ENSG00000236398	-23.7884872824632	0.0339178520847889
ENSG00000240505	-16.1968400674452	0.043591041794672
ENSG00000241697	-20.2541827541828	0.0197473266150249
ENSG00000243646	-15.8593909666871	0.0498537960889873
ENSG00000243943	-13.5289634146341	0.00548177529708554
ENSG00000244187	-12.7288319237544	0.000563775169064139
ENSG00000244187	-20.4971229760471	0.00570246594908727
ENSG00000254995	-12.3358585858586	0.00423793375162113
ENSG00000254997	-17.9655870445344	0.0315032058089109
ENSG00000255221	-25.547055684042	0.036555069792132
ENSG00000255690	-11.6808149405772	0.0189770213776895
ENSG00000255690	-12.3504896041879	0.000512147430381347
ENSG00000256463	-16.3964019723133	0.0248820738071412
ENSG00000256463	-21.898750249406	1.95468984574037E-06
ENSG00000256463	-24.0959541711421	0.000163854290307613
ENSG00000257520	-13.5327327327327	0.0236714264555738
ENSG00000258388	-15.437030075188	0.000881217599989722
ENSG00000258388	-12.5576953684546	0.0151972472985044
ENSG00000258644	-25.126213592233	0.0333275081725526
ENSG00000260596	-32.0075757575758	0.000264090097761395
ENSG00000262481	-25.2622377622378	0.0374908539061022
ENSG00000265681	-27.8483245149912	0.0397619153720593
ENSG00000267001	-19.2689677629437	0.0139942362377622
ENSG00000267110	-21.4364035087719	0.000722902618995026
ENSG00000267335	-24.5206349206349	0.00395336958051468
ENSG00000267477	-42.1052631578947	0.00358926842407119
ENSG00000267552	-18.7379567745855	0.00601386696065428
ENSG00000267631	-24.5206349206349	0.00395336958051468
ENSG00000267748	-11.7440499414748	0.0351157095258298
ENSG00000268163	-17.6767676767677	0.0134216004209188
ENSG00000268163	-20.2912102591504	0.0247558735443318
ENSG00000270800	-10.6719405397908	0.04406634342951
ENSG00000272896	-12.7288319237544	0.000563775169064139
ENSG00000272896	-20.4971229760471	0.00570246594908727
ENSG00000273049	-11.8653524270039	0.0285551186534443
ENSG00000273154	-13.2554549434345	0.0464070147864675
ENSG00000273259	-16.4386737769534	0.0364912699901172
ENSG00000273706	-13.5100521545781	1.51867451212391E-07
ENSG00000273749	-12.1543294020032	0.000191335185544997
ENSG00000277462	-14.5836288835296	0.00349485787643516
ENSG00000277462	-13.4898365882822	0.0171288842575121
ENSG00000278685	-16.6554459502971	0.0446906038244175
ENSG00000278685	-23.0212765957447	0.0282787667085562
ENSG00000282881	-23.4083850931677	0.0226508605392879
ENSG00000283189	-10.7424071991001	0.0174515769503486
ENSG00000283526	-18.0124833163225	3.86317235533345E-06
ENSG00000283526	-19.2275318817793	4.43243451267144E-09

Table 3 (*continued*)

id	meth.diff	meth.q
ENSG00000283580	-15.6722709914199	0.025593910912043
ENSG00000283586	-10.150711301	0.0134787535587177
ENSG00000283586	-12.0691131760373	0.0371369270217128
ENSG00000284194	-12.589080993989	0.0188369897278606
ENSG00000284713	-11.5865202574782	0.0125498653646383
ENSG00000284713	-12.4206553439698	0.025610830019555
ENSG00000284906	-15.7713467817686	0.045902210404969
ENSG00000285077	-15.7713467817686	0.045902210404969
ENSG00000285471	-13.0089802670448	0.00513538343420379
ENSG00000285471	-15.86969610546	0.000385506270676657
ENSG00000288611	-10.381169344394	0.00449479933783133

Table 4
Biological function of genes with elevated methylation levels.

GO:0030308/negative regulation of cell growth
ENSG00000100739
ENSG00000166923
GO:0008285/negative regulation of cell proliferation
ENSG00000088992
ENSG00000103197
ENSG00000135956
ENSG00000140105
ENSG00000165238
ENSG00000178568
ENSG00000182636
ENSG00000183145
ENSG00000198625
GO:0007050//cell cycle arrest
ENSG00000123999
ENSG00000162670
GO:0043065/positive regulation of apoptotic process;
ENSG00000064300
ENSG00000104765
ENSG00000109906
ENSG00000120063
ENSG00000131023
ENSG00000138613
ENSG00000145779
ENSG00000171680
ENSG00000176884
ENSG00000197442
Biological function of genes with decreased methylation levels
GO:0010720/positive regulation of cell development
ENSG00000005073
ENSG00000128422
GO:0008284/positive regulation of cell proliferation
ENSG00000037280
ENSG00000105550
ENSG00000105989
ENSG00000110148
ENSG00000119630
ENSG00000135452
ENSG00000135625
ENSG00000136630
ENSG00000169057
ENSG00000169083
ENSG00000170961
ENSG00000172201
ENSG00000180818
ENSG00000181104
ENSG00000184486
ENSG00000187094
GO:0043066/negative regulation of apoptotic process
ENSG00000071054
ENSG00000101188
ENSG00000106144
ENSG00000108839
ENSG00000134259
ENSG00000143479
ENSG00000143867
ENSG00000169230

(*continued on next page*)

Table 4 (*continued*)

ENSG00000172175
ENSG00000173530
ENSG00000188389
ENSG00000197785
ENSG00000198171
GO:0050728//negative regulation of inflammatory response
GO:0006979//response to oxidative stress
ENSG00000069667
ENSG00000128016
ENSG00000100983
ENSG00000122691
ENSG00000174130
ENSG00000184470

increased expression level of genes related to the RAP1 signaling pathway played an important role in this process.

In the gene body region, there was a significant negative correlation between methylation level and gene transcription in MSCs-cocultured senescent TECs, and these genes (534 risk-related genes) were defined as BNGs (Fig. 4G and Table 6). These genes are mainly involved in biological processes such as cell population proliferation, epithelial cell differentiation and regulation of epithelial cell proliferation (Fig. 4H). However, there was a significant positive correlation between the methylation level of more genes (553 risk-related genes) and gene transcription, and these genes were defined as BPGs (Fig. 4G). Interestingly, BPGs also had biological processes similar to those of BNGs (Fig. 4H). These results suggest that methylation changes in the gene body region may not only inhibit gene transcription but may also promote gene transcription in the process by which MSCs reverse TEC ageing.

2.5. MSCs promoting the demethylation of the transcription factor NGF and then upregulating KRT17 and FOXJ1

We predicted the transcription factor binding sequences of 66 genes whose methylation levels were negatively correlated with transcription levels in the promoter region and found that 9 genes were rich in transcription factor binding sequences (Table 7). Based on the gene expression correlation and sequence analyses, we selected 4 transcription factors to construct a map of the transcription factor and target gene interactions of MSCs to reverse TEC senescence via Cytoscape (Fig. 5A). In this network, NGF is the central regulatory factor, targeting 108 genes, including many antiaging-related motifs, such as KRT17, FOXJ1. The expression level of NGF was positively correlated with that of KRT17 and FOXJ1 (Pearson's $r = 0.92$ and 0.74, Fig. 5B). Indicating that promoter demethylation is closely related to the increase in mRNA expression during MSCs reversal of TEC ageing.

Immunofluorescence analysis and RT–qPCR further proved that NGF interacted with KRT17 and FOXJ1 (Fig. 5C and D). Functionally, NGF, KRT17 and FOXJ1 were mainly involved in the proliferation of epithelial cells. KI67 showed that the proliferation ability of ageing TECs increased after coculture with MSCs (Fig. 5E). In summary, these results suggest that MSCs demethylate the NGF gene of ageing TECs and promote the expression of KRT17 and FOXJ1, to promote the growth and proliferation of ageing TECs (Fig. 5F).

3. Materials and methods

3.1. Animal

Six macaque monkeys were purchased from Kunming Animal Laboratory Center, Chinese Academy of Sciences (Experimental Animal Production License No.: SCXK (Yunnan) K2017-0003), aged

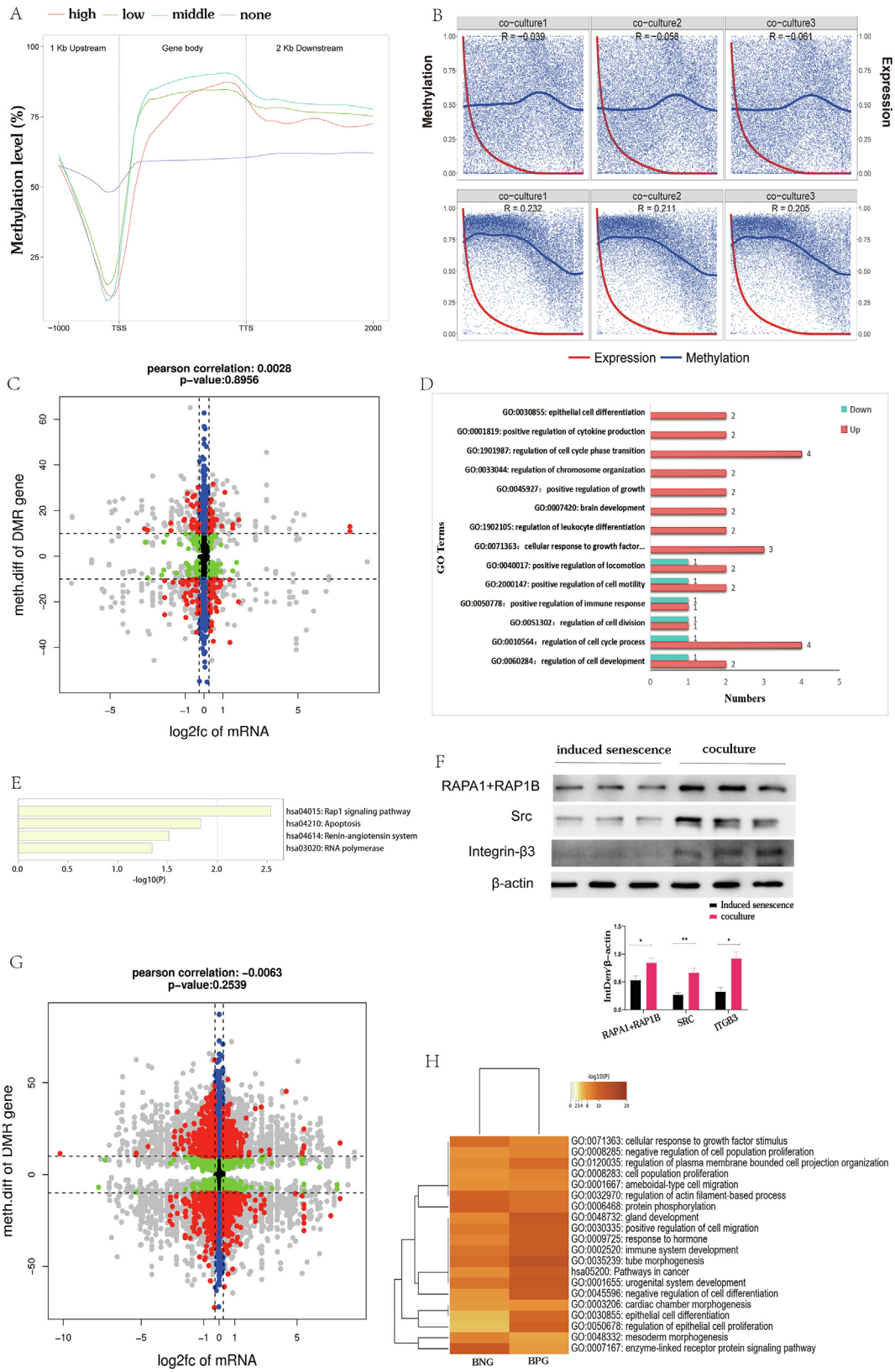

Fig. 4. MSCs regulate gene transcription by inducing DNA methylation modification. **A** In the process of reversing the aging of TECs via MSCs, the methylation level of different positions of the gene is associated with the transcriptional level (the abscissa shows different gene locations divided into upstream 1k, gene body and downstream 1k; the ordinate is the methylation level; the red curve indicates high transcription, the green represents low transcription, the blue curve represents medium transcription, and the purple curve represents no transcription). **B** Promoter (above) and gene body region (below) DNA methylation levels and corresponding gene transcription scatter plots (the red and blue curves represent gene transcription levels and DNA methylation levels in promoter and genomic regions, respectively). The horizontal axis below each box from left to right represents the level of gene transcription from high to low. **C** Nine-quadrant diagram of the relationship between DNA methylation and gene RNA-seq data in the promoter region (the abscissa is the RNA-seq log2fc value, the ordinate is the differential methylation level, and the upper left and lower right represent a significant negative correlation between promoter

22–28 years old, Weight 3.5–6.5 kg, normally raised in the Laboratory Animal Center of 920th Hospital of the Chinese People's Liberation Army Joint Logistics Support Force (Laboratory animal license No.: SYXK (Military) 2017-0051) Laboratory animal studies were approved by the Theoretical Committee of the 920th Hospital of the Chinese People's Liberation Army Joint Logistics Support Force, the approval number: 2020-034 (Section) –01.

3.2. MSCs

MSCs of macaque monkeys (BMMSCs) and human (UCMSCs) were derived from the stem cell Bank of the National and Local Joint Engineering Center for Stem Cell and Immune Cell Biomedical Technology affiliated with the 920th Hospital of the Joint Logistic Support Force. The BMMSCs and UCMSCs preserved in liquid nitrogen were rapidly thawed in warm water at 37 °C, normal saline was added, and the mixture was centrifuged at 2000 rpm for 3 min. The cells were resuspended in the DMEM/F12 culture medium containing 10% fetal bovine serum and inoculated in a culture bottle at a density of 5000/cm2, after which the DMEM/F12 culture medium was changed the next day. When the degree of cell fusion reached 85%, the cells were digested with trypsin containing 0.25% EDTA and passaged with DMEM/F12 culture medium. P4 generation BMMSCs and UCMSCs were used to determine their differentiation potential and surface markers, and the detailed methods used were described in our previous published article [19].

3.3. Cell injection

When the fusion degree of the cultured P4 MSCs generation was approximately 80%, the cells were digested and washed. They were diluted with 0.9% sterile sodium chloride solution at a concentration of 2×10^6 cells/ml. Macaque monkeys were randomly divided into two groups: the senescence model group (n = 3) and the senescence treatment group (n = 3), After the macaque monkeys in the treatment group were immobilized, MSCs were injected into the femoral vein at 1×10^7/kg per monkey once every other day 3 times, the senescence model group was infused with isovolumetric saline at the same time.

3.4. Thymus index measurement

Five months after the treatment, macaques in each group were fasted for 24 h. The body weight of the macaques in each group was measured (kg), and the monkeys were anesthetized with excess 3% sodium pentobarbital (1 kg/ml). The abdominal cavity was exposed, the rib cartilage on both sides was cut up to the upper margin of the thoracic cavity, and the thymus tissue was exposed below the heart. An electronic balance was used to weigh the mass (g) and calculate the thymus index of each monkey individually and the average value of each group was taken for statistical analysis. The calculation formula is as follows:

$$Thymus\ index = \frac{Thymus\ massx(g)}{Macaque\ body\ weight(kg)} \times 100\%$$

3.5. Thymus tissue HE staining

The thymus tissue was fixed in 4% paraformaldehyde solution for 24 h and then dehydrated and embedded in paraffin. The thickness of the sections was approximately 4 μm. After being treated with xylene-anhydrous ethanol-75% ethanol, the sections were sealed with neutral glue. Sections were observed and photographed with a Nikon microscope (NikonDS-U3, Nikon, Japan).

3.6. Determination of thymosin α and thymopoietin levels

Five months after cell injection, 5 ml of blood was collected from the femoral vein into a heparin tube and centrifuged at 2000 rpm for 10 min, after which the obtained serum was transferred to a microcentrifuge tube. The expression levels of thymosin α and thymopoietin in the serum were measured by ELISA kits (Millipore). The procedure was performed according to the reagent instructions. The absorbance (OD) of each well was measured at a wavelength of 450 nm in sequence. The measurement was carried out within 15 min after adding the termination solution. With the concentration of the standard product as the horizontal coordinate and the OD value as the vertical coordinate, a standard curve was drawn, and the corresponding concentration was determined according to the OD value of the sample multiplied by the dilution factor, which was the actual concentration of the sample.

3.7. Detection of P16 expression by immunofluorescence staining

The thymus tissue was fixed in 4% paraformaldehyde solution for 24 h and then dehydrated and embedded in paraffin. The thickness of the section was approximately 4 μm. Primary antibody Rabbit anti-monkey antibody P16 (Serviceebio:GB111143) was added for staining. FITC goat anti-rabbit was incubated at room temperature for 50 min, and the nuclei were restained with DAPI for 15 min. Finally, the sections were sealed with anti-fluorescence quenching sealant and photographed under a microscope (Nikon DS-U3, Nikon, Japan).

3.8. Immunohistochemical staining of the thymic epithelial cell-specific marker molecule CK14

Thymus tissue sections with a thickness of 4 μm were dewaxed in water for antigen repair and blocking of endogenous peroxidase. Primary antibody Mouse anti-monkey antibody CK14 antibody (Servicebio: GB12803-100) was used, and the second antibody was labeled with HRP. After incubation with the secondary antibody, the nuclei were stained with DAPI (Servicebio: G1012; DAPI dyeing: The slides were placed in PBS (pH 7.4) and washed by shaking on a decolorizing shaker 3 times for 5 min each. DAPI dye was added, and the samples were incubated at room temperature for 10 min in the dark. Sealing: The slide was placed in PBS (pH 7.4) and washed by shaking on the decolorizing 3 times for 5 min each. Anti-fluorescence quenching sealing tablets were used.). Sections were observed and photographed with a Nikon microscope (Nikon DS-U3, Nikon, Japan). The positive area signal was analyzed by ImageJ software (NIH, Bethesda, MD).

methylation and the transcriptional level). **D** GO enrichment analysis showed that the level of DNA methylation in the promoter region was negatively correlated with gene expression (ordinate: GO term, abscissa: number of genes; red indicates upregulated genes, and green indicates downregulated genes). **E** KEGG enrichment analysis of genes with decreased methylation levels. **F** The expression of RAPA1, SRC and ITGB3, the key proteins of the Rap1 signaling pathway (the measured values represent the mean ± standard deviation (`X ± s) of three replicate experiments. **P < 0.01, ***P < 0.001). **G** A nine-quadrant map of the relationship between DNA methylation and gene RNA-seq in the gene body region (the abscissa is the RNA-seq log2fc, and the ordinate is the differential methylation level). **H** In the gene body region, the DNA methylation level was negatively correlated with gene expression and positively correlated with enriched GO terms (BNG indicates that the methylation level was negatively correlated with gene expression; BPG indicates that the methylation level was positively correlated with gene expression).

Table 5
Promoter methylation is negatively correlated with gene expression.

id	meth.diff	meth.q	gene_fc	gene_p
ENSG00000169393	12	0.0493167198534707	-3.16992500144231	0.0182157396451062
ENSG00000140279	11.3766298330057	0.0425112978457713	-3	0.0192457689020148
ENSG00000183496	14.5393689412893	0.000320527649816425	-1.77258950389693	0.00215297544876282
ENSG00000166147	15.6619833863194	0.0468581371125151	-1.07480383893417	5.03157126804725E-30
ENSG00000138735	16.2222222222222	0.0350319355454426	-1.03585333801322	7.42879931992132E-58
ENSG00000178568	27.5180140945443	1.07565396326703E-07	-0.888968687611259	0.0032937298473144
ENSG00000221890	22.6050420168067	0.0345626215065825	-0.690795412733281	0.0176007089136136
ENSG00000143412	12.5132555673383	0.0244041195439192	-0.651006139135347	3.21495919043423E-06
ENSG00000145536	15.5727366159021	0.0089577681604829	-0.64965904943743	2.45479952909829E-05
ENSG00000188153	12.1476617552851	0.0439126087216701	-0.616462780545589	5.88521426071701E-15
ENSG00000167861	25.9545923632611	0.00358556744024635	-0.600339911716719	1.51057836248098E-06
ENSG00000198691	16.1113699906803	0.0178381603850453	-0.587156714134073	0.000809594934608358
ENSG00000138336	21.8070362473348	0.000861502987558523	-0.587007426706185	0.000973023962220727
ENSG00000101751	15.6150627615063	0.00847306283066711	-0.556330347365361	0.00314889263219378
ENSG00000197321	26.6782608695652	0.0141433998222048	-0.501773106156611	5.87968999963141E-08
ENSG00000184731	13.2576254294631	0.0104233490346365	-0.431430376467744	9.26373589126763E-08
ENSG00000164920	13.8862559241706	0.00141583621004862	-0.390157290173661	4.66508235306963E-06
ENSG00000196498	23.0205156060669	5.350072520849E-05	-0.365364917610353	0.0024253152303974
ENSG00000110628	12.6218323586745	0.000905019819790039	-0.364197318260097	0.0233052964014367
ENSG00000111271	14.5110267534346	0.0359526622537845	-0.353001616041892	0.00560907003355677
ENSG00000149639	12.1855383969921	0.0160852095767229	-0.347636760659084	0.00218329338042741
ENSG00000170561	12.7706888335892	0.0391539116619081	-0.347476890469923	0.00333298319309075
ENSG00000224051	30.1339896089691	0.0291683709558524	-0.322945709676845	0.0220990443969277
ENSG00000175155	22.7486965589155	0.0111237785068831	-0.313192706891764	0.00257815783289071
ENSG00000185896	20.1874052638832	0.024131183824719	-0.270676478852593	1.05874659873463E-05
ENSG00000134259	-19.9652777777778	0.00459426665426082	1.83064557204383	0.00941141544514754
ENSG00000138944	-37.8117457763475	0.0169445660029793	1.37586690199816	0.00219311995651581
ENSG00000101216	-10.3382163724572	0.0370962647151181	1.35675568344045	1.7949955026023E-14
ENSG00000119630	-10.7784431137725	0.00695950565232784	0.888209174542443	0.00320217443092626
ENSG00000129654	-10.6407004024644	6.26010353840451E-06	0.795729596937978	0.0271087679454225
ENSG00000142273	-19.4395149364094	0.0341414149043605	0.74612559345168	0.0088904789182297
ENSG00000165799	-19.8527720266851	0.0447136844752293	0.678071905112639	0.0177003751106127
ENSG00000157193	-10.0792079207921	0.00307962939304754	0.666209101707102	5.04376339464156E-11
ENSG00000181104	-13.6891228909896	0.0435232730481889	0.621100205187945	3.5853266552734E-08
ENSG00000143479	-13.636249655207	0.0401229285764378	0.606004916283042	0.00637638237944121
ENSG00000128422	-13.7385720060132	0.0117581512531377	0.539551979134848	2.51234780697392E-20
ENSG00000005189	-14.1243862520458	0.0117387368539422	0.529489164822724	7.66287517170509E-05
ENSG00000163565	-11.0395892164983	0.00942619045704688	0.515773668044346	0.000690038898638332
ENSG00000037897	-13.2831444200079	0.0266330771143665	0.513225279513817	0.00221165164613025
ENSG00000188807	-14.1644210192597	0.00214158534118136	0.50354766909851	2.372630415506E-05
ENSG00000134686	-16.0714285714286	0.0353876886095324	0.49406131874452	5.10831089048732E-11
ENSG00000123130	-37.3015873015873	5.00924521270897E-06	0.489750774803252	0.00176615938851862
ENSG00000156398	-13.6112071947423	0.0442108996079291	0.487008729785849	0.0128476275418884
ENSG00000167470	-10.062893081761	0.0449721395775338	0.476336091099384	5.09652754620344E-09
ENSG00000173530	-16.4157644250816	0.0412017199604227	0.468398314663583	0.000143462486375593
ENSG00000167523	-16.751269035533	5.8315626359607E-08	0.464668267003444	0.0158976675818633
ENSG00000118985	-15.2974664454833	0.0372468840756965	0.409987808996061	4.97570168541322E-07
ENSG00000184445	-28.9085545722714	1.10468522189305E-19	0.397728662866405	9.03292391205679E-06
ENSG00000167513	-18.2418326468431	0.00513538343420379	0.395126956365581	3.04930833769411E-05
ENSG00000113356	-30.4485219164118	0.0128237638132768	0.390375445044573	0.0389512379357209
ENSG00000273706	-13.5100521545781	1.51867451212391E-07	0.389539574228011	0.0429548369026055
ENSG00000196923	-10.1846285959639	0.0125269750370792	0.375828051950098	0.00067391254848192
ENSG00000087269	-11.5588273279091	0.0292988774562968	0.359962553043222	0.00139454612866975
ENSG00000003400	-13.0225905823676	0.0261886189599571	0.357439579522302	0.00293504239997059
ENSG00000172175	-13.6658199347632	0.0450575089860559	0.341152662152261	0.0324220388410544
ENSG00000127586	-23.5960889504197	0.0106052756412346	0.339380789036883	0.0444323090993345
ENSG00000169230	-22.6702952333828	0.0422632036507693	0.314585152068477	6.08022403373139E-07
ENSG00000197451	-11.3869559539578	0.00256448161697349	0.309912043537486	6.84334406811732E-06
ENSG00000131620	-23.3758708893317	7.69815899489769E-05	0.303751434937819	0.00347391075687533
ENSG00000132773	-18.0035650623886	0.00122867731832998	0.287830317680935	0.0230792818269578
ENSG00000172009	-24.4159883528555	0.00479288133087388	0.287040237001174	0.00229691390720688
ENSG00000142731	-21.0726198609492	0.000484552422247172	0.282650503348821	0.00173861229602644
ENSG00000204599	-15.4369398207426	0.0188931632771714	0.27892876502747	0.0479497582826186
ENSG00000171824	-12.1212121212121	0.0220298071571259	0.276012259832004	0.00631234215092042
ENSG00000165688	-12.2080440996325	1.88001695122534E-05	0.27115480052629	0.000390441450012896
ENSG00000285077	-15.7713467817686	0.045902210404969	0.266423004081944	0.0468961829118312

3.9. TECs

TEC (species: human) is a standard cell line obtained from Meisen CTCC, Catalogue No.: CTCC-004-0022p2. After the acquisition, DMEM/F12 medium containing 10%FBS was used in our laboratory for passage culture. The growth morphology of the cells was cobblestone. Meanwhile, EPCAM, a specific marker of high expression on the surface, was identified by immunofluorescence, which was consistent with the standard TEC reported in the literature, and the accuracy of the cells was confirmed (Supplementary Fig.1).

Table 6
genebody methylation is correlated with gene expression.

id	meth.diff	meth.q	gene_fc	gene_p	
ENSG00000140379	17.1726137641281	0.0460288318272713	7.75933340719466	0.0367406623189661	BPG
ENSG00000198626	24.7863247863248	0.0428569231124602	5.4374053123073	0.0297721172788166	BPG
ENSG00000273217	12.0838262633091	0.0017609206903326	5.32192809488736	0.0445013525732622	BPG
ENSG00000185339	45.2941176470588	0.0247584438639287	4.3037807481771	0.00178271206325163	BPG
ENSG00000047457	13.4175878772823	0.0283611057261894	3.22994977251453	1.66788126916758E-24	BPG
ENSG00000288520	36.7167919799499	0.00179587138482442	2.7004397181411	0.0288626152504842	BPG
ENSG00000152953	35.8585858585859	0.0108455530672616	2.32192809488736	0.0352806015308715	BPG
ENSG00000197641	12.020202020202	0.0382074798208661	1.92619869958988	1.92719648884193E-25	BPG
ENSG00000198768	10.8635026873542	0.0455223482400552	1.91753783980803	0.0395432526802723	BPG
ENSG00000149557	30.7784252203795	0.0362978205542385	1.73142547723426	1.52589890721511E-08	BPG
ENSG00000081985	21.5675057208238	0.0323846219542733	1.72582503656101	0.0427904082297945	BPG
ENSG00000162711	17.6871052985175	0.000259725399986543	1.53605290024021	2.06547568623394E-07	BPG
ENSG00000259207	19.1260923845193	0.0176749247514635	1.49185309632967	5.16678595835762E-10	BPG
ENSG00000139278	10.7863631180875	0.000163880514573194	1.40892736291598	1.16755566875088E-14	BPG
ENSG00000154678	18.3439422018102	0.0436144473018669	1.39854937649027	0.0282987501155144	BPG
ENSG00000130164	21.9712015888779	0.0293316809944489	1.38476472870143	1.68437434910057E-68	BPG
ENSG00000288602	10.0578466131741	8.69490707846433E-06	1.38133628405012	1.22193778792156E-06	BPG
ENSG00000101216	14.0663390663391	0.00599990842666912	1.35675568344045	1.7949955026023E-14	BPG
ENSG00000163485	22.2225941422594	0.000337583593079858	1.34513548604869	0.0424124417976442	BPG
ENSG00000188001	19.9379675241744	0.0462884117852547	1.33763299559323	1.51293275212706E-05	BPG
ENSG00000090339	21.8632075471698	7.55280953546309E-10	1.22517486200778	1.17341214937116E-27	BPG
ENSG00000196639	10.9243697478992	0.0226627811165279	1.12687176584051	2.79229839886979E-11	BPG
ENSG00000002587	12.3692427790788	0.0030212729838875	1.09953567355091	0.00241065519046194	BPG
ENSG00000167914	24.1176470588235	0.00878621065548137	1.0790715709912	0.00212095639712	BPG
ENSG00000255398	10.5249083129584	0.00555500233808119	1.0759488532333	0.0213799392158058	BPG
ENSG00000124496	11.8697478991597	0.0197051200937206	1.05475976867859	9.74227997345186E-09	BPG
ENSG00000185022	21.4285714285714	0.00027811976367497	1.03023961317768	4.14560461289623E-22	BPG
ENSG00000112096	14.5454545454546	0.046217877185254	1.00829655641631	0.0277179645543597	BPG
ENSG00000138316	17.4206525733516	0.0304301935480177	1	0.00942259240403998	BPG
ENSG00000118515	11.5896851801896	0.000186787297261282	0.986540356802792	1.56070357468565E-40	BPG
ENSG00000125730	22.6524064171123	0.0001539492364998	0.940197017497937	1.10578488599274E-13	BPG
ENSG00000164120	28.8961038961039	0.0361783351821684	0.934782340553516	0.0395141713878454	BPG
ENSG00000163568	11.2735708508918	0.0279618332417633	0.931046368249858	7.94510291344592E-10	BPG
ENSG00000182752	27.8974358974359	0.0415386692927686	0.883355081147731	1.45670435422431E-15	BPG
ENSG00000111700	10.3794923347575	0.0474623507181872	0.867939147909315	0.0025682878525908	BPG
ENSG00000100379	10.7658959537572	0.015640943861462	0.8600179616186	3.78521809513934E-05	BPG
ENSG00000198121	11.5673799884326	0.000235463010867662	0.853133922996195	2.54618474694495E-12	BPG
ENSG00000129521	25.5984555984556	0.0222067965182979	0.84358980503217	2.59806804251617E-05	BPG
ENSG00000100060	21.0711768851304	0.0106912163846665	0.828631581688019	0.0273481690302178	BPG
ENSG00000075131	19.4487577639752	0.0424731991250545	0.816530118457942	0.00474497942871165	BPG
ENSG00000114541	28.8600288600289	0.0474421974610935	0.815747086313056	1.42922170794235E-22	BPG
ENSG00000174640	16.9152167909417	0.0387405060017022	0.800012946716431	0.00209466071836222	BPG
ENSG00000129654	16.5985021511659	0.0298086831017226	0.795729596937978	0.0271087679454225	BPG
ENSG00000156299	22.9379548628979	1.07161511929475E-05	0.792603966282472	5.65041318074885E-06	BPG
ENSG00000105137	10.7254534083802	0.04654172520713	0.786429083203057	0.000279118337134963	BPG
ENSG00000095303	16.1793847253354	0.0211069184576635	0.764794459829562	1.5199467943708E-06	BPG
ENSG00000134954	23.1418370658877	0.0277963868963604	0.761605766840066	2.56715039043354E-44	BPG
ENSG00000103546	16.2875313398153	0.00349398264893309	0.758806642705791	0.0418443211370969	BPG
ENSG00000160256	13.6070021316453	0.0214647227421257	0.753891509689743	0.0332320116864089	BPG
ENSG00000164023	21.25	0.011922179126476	0.746225542778568	0.000363807452821192	BPG
ENSG00000123358	15.8217347220942	2.16626464371985E-05	0.737561626003184	5.9249188956385E-06	BPG
ENSG00000157654	15.244622339966	0.0376927615809148	0.735084635567444	0.00032002751951902	BPG
ENSG00000104856	25.2747252747253	0.000251979891967708	0.724771694854199	1.12785792226896E-07	BPG
ENSG00000138829	38.4102564102564	0.0495299856395462	0.713477241243836	0.0417689085213096	BPG
ENSG00000198517	10.0071965456581	0.000250857317643525	0.710892082556315	1.95937520854343E-12	BPG
ENSG00000140525	12.7136879856545	0.0492349249753731	0.703928500914718	1.88197511468814E-10	BPG
ENSG00000034152	26.2759170653907	0.00144846259665856	0.693086631049928	5.24816371136761E-05	BPG
ENSG00000213397	26.1435608726249	0.0272650692982965	0.689932060322699	0.000404367736333311	BPG
ENSG00000184408	26.011760636458	0.039074500980129	0.667424660913128	0.0384781428522723	BPG
ENSG00000077238	12.7857142857143	0.00257455533047546	0.662159614919003	1.55807095924066E-27	BPG
ENSG00000116396	26.0964408725603	0.0096893888071383	0.657112286476989	1.35258473501439E-06	BPG
ENSG00000145220	23.3350488934637	0.00284511941794192	0.652682641836568	0.000888214720779499	BPG
ENSG00000135074	28.6655462184874	0.00818970336907842	0.650885862801071	1.17888754456392E-37	BPG
ENSG00000008517	14.6666666666667	0.0123730750888345	0.648782870854652	0.0124472970165069	BPG
ENSG00000134070	16.1204481792717	0.0327234089529168	0.642404392962848	0.00154731554224759	BPG
ENSG00000130066	19.1561875661065	0.0406547451253858	0.639525806945979	0.000483308213269925	BPG
ENSG00000115109	17.8514588859416	4.29516076726877E-06	0.631074425575469	0.0210371778011025	BPG
ENSG00000006432	28.8508118776352	0.00145775249728922	0.629872816855305	2.88466436771349E-27	BPG
ENSG00000126091	12.0560248048754	0.0298997792651608	0.626850897011178	0.00839083915114877	BPG
ENSG00000185033	12.3076923076923	0.0246845329093198	0.625898044084284	2.59811443497528E-21	BPG
ENSG00000073756	11.7949854686961	4.76806497395308E-10	0.624200327276437	4.92058830388309E-17	BPG
ENSG00000127666	20.7014835777378	0.0361625798985242	0.617666665793861	2.82406615980706E-06	BPG
ENSG00000171612	10.2189781021898	0.0299114399803943	0.616403847923919	3.85613698182859E-06	BPG

(continued on next page)

Table 6 (*continued*)

id	meth.diff	meth.q	gene_fc	gene_p	
ENSG00000188352	14.4671841919548	0.0234512792736483	0.616017225301995	1.77958293421601E-09	BPG
ENSG00000154217	10.3516533749092	0.000322810648896246	0.615899482470343	0.000662697989781469	BPG
ENSG00000112159	14.5891528611334	0.015561117088738	0.610708775591004	0.00592967658047154	BPG
ENSG00000143479	19.2099637918248	0.0216185651681438	0.606004916283042	0.00637638237944121	BPG
ENSG00000250021	11.3825232938806	0.0240344121618717	0.593732710348888	0.00848014211495732	BPG
ENSG00000128294	10.5763517528223	0.00140043111047096	0.59321592735501	0.0345827448979271	BPG
ENSG00000154655	18.9600840336134	0.0123963264712088	0.59183345241	1.03930323127386E-06	BPG
ENSG00000165650	18.3908045977011	0.0015304926249123	0.579453598291972	0.0453755163033109	BPG
ENSG00000179583	23.2768127929418	0.0270751116053932	0.577751585826059	0.000353913888725189	BPG
ENSG00000140945	37.7016129032258	0.00981463319013045	0.574978412148533	0.00366332390862918	BPG
ENSG00000128578	10.0450605262153	0.0130192453752586	0.574341384964587	0.00284139827758737	BPG
ENSG00000131941	19.8850447662209	0.00447847862477616	0.573258396588686	1.74407845148977E-14	BPG
ENSG00000175832	11.9083269671505	0.0394262915203526	0.571278916880122	0.000200810502007593	BPG
ENSG00000166444	17.8225806451613	0.0194673305790636	0.56545984417481	4.99627819602438E-09	BPG
ENSG00000156113	26.7635590216235	0.0105659788754113	0.562791119722535	0.0227562050853387	BPG
ENSG00000142185	51.7641129032258	8.09380543598331E-08	0.561438218660123	0.0293332076847108	BPG
ENSG00000145675	22.5126646403242	0.0137608208710987	0.55549389265715	0.02168041321141	BPG
ENSG00000133773	23.4776987718164	0.0497599820915567	0.553529152545131	0.0232769540006936	BPG
ENSG00000115641	17.0194508009153	0.0110685012966746	0.552391837873705	1.0526762753976E-29	BPG
ENSG00000060558	13.75	0.0266218044809461	0.550616755318472	0.00025669154956774	BPG
ENSG00000147065	29.0869916509561	0.0240709907229761	0.53654301642417	8.11287354734939E-30	BPG
ENSG00000110427	36.6200578592093	0.0122666642572542	0.532060599558595	0.00291374882581983	BPG
ENSG00000159200	13.9405684754522	0.0441669320419815	0.529082695095812	7.08904757466765E-07	BPG
ENSG00000116120	13.2267732267732	0.0344536764202843	0.528875755953478	0.00805916733707207	BPG
ENSG00000162419	27.9619805481874	0.00685307479690918	0.525155335489124	0.00223599875365847	BPG
ENSG00000167670	21.763859832636	2.73646856659351E-07	0.521039303621415	0.000147383634918683	BPG
ENSG00000005884	22.8070175438597	0.0402615281928553	0.513443633410088	3.7351721134188E-23	BPG
ENSG00000171488	17.1157687795288	3.2058714522525E-07	0.513239813177653	0.00114332064975316	BPG
ENSG00000073712	12.5	0.0341240726600526	0.512037234330269	1.28218578484813E-07	BPG
ENSG00000137309	15.2883630986236	0.00729589058035453	0.511487559636413	4.36463899514817E-15	BPG
ENSG00000125731	17.948717948718	0.0396708027087845	0.509667175183969	0.00391499527626842	BPG
ENSG00000196792	12.5	0.0439863781029824	0.507954281998884	0.0461085059867358	BPG
ENSG00000101773	27.5862068965517	0.0387651384224958	0.506702061037264	1.17953929546148E-06	BPG
ENSG00000134686	11.9293924466338	0.0319547070303023	0.49406131874452	5.10831089048732E-11	BPG
ENSG00000125454	16.9843160611475	0.0163651212626911	0.494043665158886	0.00543931724489655	BPG
ENSG00000285901	11.6166587674845	0.0444463457358793	0.485665901665924	0.00265331917593365	BPG
ENSG00000075702	23.7220969376083	3.0737873482305E-10	0.484470132810983	0.0150733519063799	BPG
ENSG00000039560	13.9867156739778	0.00138145335108338	0.483171930628531	6.66514055683011E-11	BPG
ENSG00000168970	11.4285714285714	0.0459755722858929	0.48275764039426	0.0452815641249222	BPG
ENSG00000100023	12.4508215690812	0.0133970134671646	0.482668327207678	0.0105207229595894	BPG
ENSG00000132334	12.1472244811903	0.0474686841805455	0.475178385333266	7.6377217442228E-05	BPG
ENSG00000073282	11.9007689143436	0.048546782398754	0.473557736578936	0.00196863331449595	BPG
ENSG00000177706	17.7135047693423	0.00787495879534455	0.471523213919535	5.28191185180264E-07	BPG
ENSG00000100065	26.4326432643264	0.0191484913378948	0.470268230654617	3.15996374866782E-08	BPG
ENSG00000198042	17.7547169811321	0.0232281921397903	0.468902336950411	8.33417033982992E-09	BPG
ENSG00000173530	10.1123595505618	0.0384166465261006	0.468398314663583	0.000143462486375593	BPG
ENSG00000137478	15.511611030479	1.51079661917468E-05	0.46837326134002	0.00725447648208387	BPG
ENSG00000171132	24.9302501536861	0.0160456878041116	0.468248157279246	0.0072417886941382	BPG
ENSG00000149177	10.7246688919996	0.00630639306502788	0.467617414400212	0.0446129236346782	BPG
ENSG00000113643	10.2938593409682	0.00576526528660252	0.46607475129958	0.0101843122334553	BPG
ENSG00000109320	15.1220905326289	0.00163633849319427	0.460363788572407	6.35552267042898E-06	BPG
ENSG00000134775	12.1574777154176	0.00829919587995446	0.459090918425327	3.0528769923768E-05	BPG
ENSG00000169851	21.8632075471698	0.0431605350915495	0.453708983530555	5.70757756837102E-06	BPG
ENSG00000259316	23.1493553527452	0.00128148450740161	0.451443145707578	0.0297853829323746	BPG
ENSG00000128050	14.9583297534152	0.0158462688766661	0.451141139038848	5.93185210126709E-16	BPG
ENSG00000179958	14.7819042555885	2.14522521012426E-05	0.44825768623875	3.09507657388312E-08	BPG
ENSG00000157551	11.5706200154361	0.0419093860693028	0.447594054452798	0.00230304213579688	BPG
ENSG00000163866	23.685580426861	0.049655105392165	0.44323975577384	0.000258724968656793	BPG
ENSG00000196793	11.978766501362	0.0460453262119517	0.435328215579876	0.00221912060149269	BPG
ENSG00000135763	16.8818129661503	0.0302759054994361	0.433984742554527	6.53126311486347E-08	BPG
ENSG00000092969	11.648993391732	0.0210412227946416	0.432025567700634	1.3965214654066E-08	BPG
ENSG00000081181	15.3088177871695	0.0430246629965016	0.431315577801243	0.0498940329939293	BPG
ENSG00000148459	14.4086021505376	0.048742111856042	0.429364974832301	0.0433078449692255	BPG
ENSG00000051180	16.4885639295088	0.0420749503776668	0.427558428562299	3.10366858073935E-05	BPG
ENSG00000113119	14.2857142857143	0.0395734332048679	0.424497828527911	0.02981061954876	BPG
ENSG00000100311	27.8616120721384	3.50691882283434E-07	0.424012807497665	8.81366769431761E-06	BPG
ENSG00000126261	13.347296451442	0.000867938947185886	0.421711643478361	3.50063286508391E-07	BPG
ENSG00000155903	13.953488372093	0.0018964907491042	0.42148143218127	0.0102460084903322	BPG
ENSG00000120254	10.3525152439024	0.00242563790018186	0.416225112127262	3.11356337626985E-05	BPG
ENSG00000126215	18.6881263285758	0.0047041318130588	0.416095969642456	2.96320540656788E-06	BPG
ENSG00000159131	20	0.0337146988601268	0.414334455978619	1.40212757091001E-07	BPG
ENSG00000197903	11.3590263691684	1.80362232316675E-09	0.410538463717116	7.24747897837557E-06	BPG
ENSG00000166949	19.5793163891323	0.00299223158104252	0.410357367727777	6.43088240364512E-15	BPG
ENSG00000100504	11.4035087719298	0.0278155256641892	0.405476621878327	3.69273681550957E-06	BPG
ENSG00000189306	15.6716417910448	0.00152601710196405	0.404623362222909	0.000214579136064702	BPG

Table 6 (*continued*)

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ENSG00000139083	19.1780821917808	0.00773957494205465	0.400130877301734	7.7711291486059E-05	BPG
ENSG00000184445	10.5769230769231	0.00114852995589866	0.397728662866405	9.03292391205679E-06	BPG
ENSG00000105202	10.0411123165648	0.0330650395447605	0.395966085873695	6.31028858614087E-11	BPG
ENSG00000156787	12.1844018914281	0.0393350703880211	0.395736943319907	4.74318720256828E-05	BPG
ENSG00000053747	10.6796116504854	0.0249529707542088	0.395144257913057	7.61837371152048E-10	BPG
ENSG00000115355	13.1376409522105	0.0487519118431527	0.391856276845191	0.00256243902236652	BPG
ENSG00000013573	24.5015576323988	0.00653446009730904	0.390982972113944	5.35715606980235E-06	BPG
ENSG00000180198	14.5269770879527	0.00763746153955366	0.385403936585871	1.18342807408686E-09	BPG
ENSG00000115946	11.3475177304965	0.00367585685707775	0.385224026927863	0.000480076541409388	BPG
ENSG00000012048	13.0100374175922	0.00926282151959503	0.381249185822562	2.9090055172466E-05	BPG
ENSG00000160294	14.3973673385438	0.0219556763363379	0.381127688585386	0.044429515549183	BPG
ENSG00000173744	11.8819776714513	0.00871363348299071	0.379563150298012	0.00111750633730919	BPG
ENSG00000119969	17.910447761194	0.00623376601063658	0.379206507287822	0.000129620391717274	BPG
ENSG00000111145	10.3885590933621	0.0252251574384709	0.378221079492621	0.000425935635161594	BPG
ENSG00000276043	15.2073732718894	3.37152560029063E-05	0.377966627324228	1.13351188388114E-08	BPG
ENSG00000131759	15.3109619686801	0.045316903961093	0.376819201869858	0.000596980581262559	BPG
ENSG00000020426	33.2469029098243	0.0497208468729494	0.372042127924171	0.0012578498521631	BPG
ENSG00000072110	27.020202020202	0.0420260837507448	0.36814862841075	2.13959571937118E-10	BPG
ENSG00000169299	15.2948717948718	0.00130471132303523	0.366885877093739	0.000144955318663788	BPG
ENSG00000174501	11.8978243978244	0.0228953502973815	0.36513259345253	0.00490678291116583	BPG
ENSG00000154743	11.0578174381855	0.0153407685857562	0.360511380098629	0.00516434764538364	BPG
ENSG00000143514	16.5490338683284	6.71877076986303E-10	0.35881789621363	2.17092794895104E-06	BPG
ENSG00000111424	11.2359550561798	0.0317962645934882	0.358662099457706	0.00294175959312844	BPG
ENSG00000108559	17.9736352881528	0.0417143548284744	0.358475087047095	4.28853145568068E-09	BPG
ENSG00000197971	17.0625	0.0140844301130111	0.357679336817535	3.79081187181759E-06	BPG
ENSG00000151693	11.0769230769231	0.000658666735123762	0.354638036216122	4.57279940276897E-06	BPG
ENSG00000143228	14.4578313253012	0.0208397804233328	0.352493102853737	0.0200404463308018	BPG
ENSG00000140854	13.9843332739897	9.17285896260538E-05	0.351879441055567	0.00121403316807806	BPG
ENSG00000129514	12.5007845352413	0.00577489664804183	0.351208674792523	0.000144498645147243	BPG
ENSG00000111716	18.602383531961	0.0119289900082757	0.349363197618885	7.78544029694051E-09	BPG
ENSG00000171960	11.9368414184582	0.0104242592834035	0.347761011385615	0.000726796975151203	BPG
ENSG00000165244	12.4912016088487	3.86317235533345E-06	0.34696056772625	3.9169520938833E-05	BPG
ENSG00000080823	10.9767692453966	0.00130393296666201	0.344892675250566	0.00398579795922971	BPG
ENSG00000172175	10.8527394935162	0.0194774047441644	0.341152662152261	0.0324220388410544	BPG
ENSG00000159259	10.5882352941176	0.0489008832325082	0.340424438504752	0.00145586742134146	BPG
ENSG00000159128	25.1612903225806	0.0485527510449985	0.337842993482334	7.27318213579374E-05	BPG
ENSG00000110047	24.1612461485793	0.00150776844036724	0.334528870269943	0.000109902689365428	BPG
ENSG00000197063	11.8755328218244	0.0493378159714684	0.334400889337693	5.31922911707779E-05	BPG
ENSG00000221968	21.5480150809492	0.031818947144702	0.334384137494428	0.00343241815016781	BPG
ENSG00000179115	11.0260946483857	0.0294813144269249	0.334306506654892	4.75012410699513E-05	BPG
ENSG00000115163	11.7391304347826	0.00059433024365012	0.332183719875603	0.00177234839493096	BPG
ENSG00000213024	14.8489314664701	0.0235226165595666	0.331862529986476	0.045445417558425	BPG
ENSG00000111252	16.9539752922486	0.00573589684459279	0.33125115813949	3.52825565234949E-05	BPG
ENSG00000145819	14.3424599233934	0.00230343250039912	0.330677158225405	0.00536155887245511	BPG
ENSG00000102144	10.3479853479854	0.011765225239976	0.330116832106607	2.36274902194076E-07	BPG
ENSG00000140859	15.2478537801163	0.00284421553068667	0.330101558567158	0.000308947762721306	BPG
ENSG00000185238	15.3594273530308	0.000471869346833329	0.329647926677459	9.70284664586077E-05	BPG
ENSG00000196535	19.5542652207326	0.00197961366255126	0.328931310926499	0.0123758316344305	BPG
ENSG00000173200	15.7881024750326	0.00412154700403832	0.328436881055434	0.0279958714637936	BPG
ENSG00000062038	10.9421972381767	0.00574831964808328	0.328215850647634	2.00014818397733E-10	BPG
ENSG00000092853	11.5196078431373	0.012374369365079	0.327634213232578	0.000642703698649307	BPG
ENSG00000145216	15.7894736842105	0.0471230922301574	0.327626700219808	0.00607568903684875	BPG
ENSG00000077348	15.830964073404	0.00108924937474028	0.326243984244442	0.0280479451978743	BPG
ENSG00000137656	10.2321516774953	0.00452774440080063	0.325524575166875	0.00429430569035293	BPG
ENSG00000076248	14.6496976872014	0.0407787165171559	0.32454088468853	4.47249577241696E-06	BPG
ENSG00000136237	22.4313725490196	0.012350922476546	0.321138596741079	4.02880506756189E-05	BPG
ENSG00000104852	12.5020698791191	0.0227116726783726	0.320980373575367	0.0272299406051771	BPG
ENSG00000104626	20.1738473167045	0.0483717092209023	0.319384146212676	0.00182257271468747	BPG
ENSG00000165304	12	0.020179851199169	0.319129648728101	2.3370565052397E-05	BPG
ENSG00000214113	21.1263579188107	0.000236248660011793	0.31875051786639	0.0469611212957108	BPG
ENSG00000138442	33.6170212765958	0.032344777797837	0.318574659777552	4.27600892666218E-05	BPG
ENSG00000186871	19.3867020492408	0.0102955415871951	0.318210088479527	0.000680436735418216	BPG
ENSG00000107954	25.7726558407543	0.00123449997198655	0.313660478903761	0.000112848217085662	BPG
ENSG00000049541	10.2450498225206	0.000400881435876873	0.31359405800916	0.0156478701318847	BPG
ENSG00000122359	11.6279069767442	0.00253084737125586	0.312801510270879	0.000137209904272935	BPG
ENSG00000179262	22.7272727272727	0.0383036857631157	0.309587279210015	0.0168093082757781	BPG
ENSG00000166451	15.7765303394814	0.0013292853894967	0.306754469098701	0.000145665072772221	BPG
ENSG00000105486	11.1876709446665	0.03642502559154	0.30478296776648	0.0373791119128896	BPG
ENSG00000104835	11.9350282485876	0.00336520016079593	0.303755348840111	0.0495039185082071	BPG
ENSG00000160072	11.7262922619128	0.0355442426299282	0.300394933337722	0.0255083618535847	BPG
ENSG00000139618	10.8834244080146	0.0381891489049431	0.300036654668547	0.017616581598741	BPG
ENSG00000284776	23.1168831168831	2.49177149563819E-08	0.299726261915365	0.00257452786653715	BPG
ENSG00000164251	12.5490196078431	3.12802531249179E-05	0.299055569030699	2.62346645158704E-07	BPG
ENSG00000132153	13.6713422949542	0.000190494073763039	0.298366594115216	0.00132106509958911	BPG

(*continued on next page*)

Table 6 (*continued*)

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ENSG00000153179	11.509215637656	0.00487777271105144	0.292518165356911	7.62622000548776E-07	BPG
ENSG00000133119	23.297342192691	0.024796155868454	0.290809071935399	0.000710793479083628	BPG
ENSG00000171943	10.7947212855418	0.0281433704455951	0.289910858011574	0.0146448175451878	BPG
ENSG00000127080	11.6788321167883	0.0118293720940106	0.289688322543739	0.00095971556272434	BPG
ENSG00000127824	26.4705882352941	0.0319767800481153	0.289521638774619	1.71137376219558E-05	BPG
ENSG00000178409	10.7233589673167	0.000688602871074047	0.2883218952718	0.00811924789522798	BPG
ENSG00000125821	23.1168831168831	2.49177149563819E-08	0.284006254468088	0.00304151597190549	BPG
ENSG00000129911	24.0011750881316	0.0109134199611343	0.283108845996834	0.0165962119775145	BPG
ENSG00000197586	10.8916207611058	0.0240152796463978	0.281801266632194	0.000165273603573787	BPG
ENSG00000120992	12.068653815733	0.0467686393144206	0.281043679407856	0.00312991441616504	BPG
ENSG00000131373	21.502698215027	0.0348851228680506	0.280466355713528	0.026673189701079	BPG
ENSG00000183856	14.939120560217	0.00353857287210456	0.279732061639544	5.33521552830561E-05	BPG
ENSG00000074201	15.3724062113508	0.000714746368067523	0.278172389751471	0.00542221796366029	BPG
ENSG00000179889	11.6279069767442	0.0234358092629859	0.27721334100356	0.0196164217673316	BPG
ENSG00000103202	10.2702702702703	0.00299211581336382	0.276504211136244	0.0291270972475958	BPG
ENSG00000198055	17.5735294117647	0.0360027243666033	0.276497268169316	0.00122532365132121	BPG
ENSG00000129422	12.9141960237182	0.00353438535321241	0.273855899087307	0.00271216328064717	BPG
ENSG00000163293	36.5049751243781	0.0114068205386867	0.272023189061049	0.0270981163833197	BPG
ENSG00000124171	11.4952359930839	0.030251961845611	0.270512585386815	3.33325787602703E-05	BPG
ENSG00000159921	16.6319740120478	0.0247102650373921	0.268776922763959	0.0157864714181887	BPG
ENSG00000001497	12.0453190220632	0.0233246031741301	0.268705941554237	0.00102904917257424	BPG
ENSG00000103121	15.7765303394814	0.0013292853894967	0.267698066293964	0.016451034700755	BPG
ENSG00000135932	12.251837394407	0.0156600904910185	0.267400192087818	4.11766224712256E-06	BPG
ENSG00000169021	19.7987405852574	0.0331848943325761	0.266995356380579	9.14558067484257E-05	BPG
ENSG00000105011	12.962962962963	0.00398196380955524	0.265799661790176	0.000169594915789348	BPG
ENSG00000184967	13.373809622822	0.000941887320689719	0.265344566520995	0.0469442423787682	BPG
ENSG00000101255	10.6708140393795	0.00346186997238993	0.265331770942825	8.46152401667505E-06	BPG
ENSG00000159322	30.5180533751962	0.0276939285224039	0.264849727499511	0.031358037477596	BPG
ENSG00000169393	-25.3085083351375	0.00854580724472204	-3.16992500144231	0.0182157396451062	BPG
ENSG00000005108	-22.2422494592646	0.020365372525717 8	-3.12553088208386	1.24596404142175E-06	BPG
ENSG00000115738	-27.2559410725594	9.52294042593639E-09	-3.01016459334895	4.18756231129654E-60	BPG
ENSG00000140279	-17.3963133640553	0.0439791706564696	-3	0.0192457689020148	BPG
ENSG00000179044	-11.8119658119658	0.0011790794908365	-2.75488750216347	0.0455889340587114	BPG
ENSG00000198673	-21.1428571428571	0.0368537626321193	-2.67807190511264	0.0262071277264242	BPG
ENSG00000165568	-14.2735042735043	0.0119260335280958	-2.32192809488736	0.0490441201507172	BPG
ENSG00000144218	-34.3563902885937	0.0334977985633422	-2.17791779219585	1.12979214761745E-05	BPG
ENSG00000132854	-22.8348649401281	2.62412424405558E-05	-2.14498791765084	5.70477130980723E-25	BPG
ENSG00000214860	-14.752079166228	0.0357688651189397	-1.9831261814356	0.0106317837925749	BPG
ENSG00000122367	-34.6323529411765	0.0106724369520212	-1.85561009066482	0.00523883401102577	BPG
ENSG00000124766	-28.7427162707306	0.0305691015210822	-1.70659194512269	4.71764749310228E-08	BPG
ENSG00000170871	-11.2102325960324	0.0447876537542586	-1.66699826958717	4.56446949371295E-10	BPG
ENSG00000145526	-28.7231848184819	0.0150508507436879	-1.61598939634178	0.00646044956681184	BPG
ENSG00000184588	-30.9081527347781	0.0464620728183575	-1.6000299488101	3.46814360898919E-07	BPG
ENSG00000177679	-26.0307692307692	0.00289766189866405	-1.59991284218712	0.0138522073197324	BPG
ENSG00000171847	-16.6869638885947	0.0292778679893094	-1.5722514489716	0.0291208044305836	BPG
ENSG00000198734	-14.3318587177867	0.0345038617590958	-1.56021583838547	8.38227320628895E-21	BPG
ENSG00000176399	-24.8348017621145	0.000673263816959103	-1.53343220008107	0.00119524778946158	BPG
ENSG00000170962	-26.6187050359712	0.0089555471845991	-1.46948528330122	0.00328843491383136	BPG
ENSG00000096006	-15.7666894509	0.0375840981055877	-1.46733200672105	0.000154999070643722	BPG
ENSG00000117318	-22.5806451612903	9.36255404736851E-06	-1.45691426106468	9.98591828088862E-70	BPG
ENSG00000187634	-32.1937321937322	0.0194393818625017	-1.362232804096	4.32371894143658E-05	BPG
ENSG00000164292	-16.8253968253968	0.0489389998905521	-1.32775695358668	2.06829375217998E-43	BPG
ENSG00000110693	-22.723094096789	0.00434170059540129	-1.3112016882943	0.00661793779747204	BPG
ENSG00000031081	-23.1221590909091	3.85163478790826E-05	-1.30618535834161	0.0136161269955364	BPG
ENSG00000283765	-18.060221475675	0.0201026712084086	-1.27105142340771	0.00121867914175793	BPG
ENSG00000183307	-44.8542805100182	0.0122239033285652	-1.25779775746765	0.0201283284961805	BPG
ENSG00000126882	-11.474980351061	0.0431523638296012	-1.25375659224578	1.32638827271431E-05	BPG
ENSG00000125378	-17.9442875805976	0.00159035617570787	-1.22239242133645	0.00421868324091519	BPG
ENSG00000022267	-11.410411622276	0.0396008506303448	-1.17523880133878	3.55852677638216E-33	BPG
ENSG00000167080	-11.4236928221097	0.0144869300714228	-1.16753048630192	2.32961544138755E-06	BPG
ENSG00000187720	-19.4477791116447	0.0219138227172992	-1.13814629276965	0.012520318473065	BPG
ENSG00000143341	-19.5062850219597	0.0402301439644637	-1.13670923392942	6.97523100767761E-36	BPG
ENSG00000255690	-11.6808149405772	0.0189770213776895	-1.12810482574769	0.00330599810212225	BPG
ENSG00000112902	-11.6916269571137	0.00115469564699574	-1.11393198503502	1.05408010797426E-37	BPG
ENSG00000172348	-14.8290188558645	0.0136130268570052	-1.09019780897158	0.0423127348056044	BPG
ENSG00000123364	-10.5263157894737	0.000314566514861363	-1.08318591161621	1.69242220698737E-23	BPG
ENSG00000068781	-15.7183499288763	0.00516409946365694	-1.07635088613011	0.00551621832195923	BPG
ENSG00000125845	-11.3027843053479	0.00789415268806258	-1.07397404155579	5.18332620110209E-18	BPG
ENSG00000187867	-12.8241040005746	0.0116382197911919	-1.0630097975258	0.023188149041441	BPG
ENSG00000135063	-17.3875054609	0.0406662819530852	-1.05169323418149	0.00332636281879902	BPG
ENSG00000123407	-10.9556347791642	0.0142153062123272	-1.0221957461142	2.21399677099899E-11	BPG
ENSG00000178826	-12.3389400190416	0.0314189626104258	-1.00938081120952	1.33830789090272E-22	BPG
ENSG00000197183	-18.7180988179232	5.05701304476227E-05	-0.987198717776908	0.0149582145196133	BPG
ENSG00000198246	-11.7647058823529	0.0188313265083686	-0.985032424402025	4.50193522132467E-16	BPG

Table 6 (*continued*)

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ENSG00000130720	-21.4462659380692	0.00488164898792484	-0.948385892392463	0.0284975232744333	BPG
ENSG00000115425	-18.5714285714286	0.00683444399629947	-0.94727689644708	0.0299146981065191	BPG
ENSG00000130303	-28.1553015372487	2.47925168599852E-07	-0.941000038982854	1.31028864997261E-05	BPG
ENSG00000169239	-46.286231884058	0.0364241250009795	-0.931574858989118	0.0130880099341582	BPG
ENSG00000181638	-19.5980542754736	0.0055229125237	-0.899639693651051	0.000113364332831388	BPG
ENSG00000243244	-13.4214394599303	0.0460770585806583	-0.890223773079601	6.82444981046458E-15	BPG
ENSG00000151623	-27.6649369903632	0.0397955454574244	-0.888830624063527	2.85802238792563E-05	BPG
ENSG00000146197	-45.2380952380952	0.00908276863868429	-0.880701071627657	0.0107350099427185	BPG
ENSG00000274070	-11.5542845675296	0.0262921135672129	-0.880634915716104	3.61509000218277E-26	BPG
ENSG00000101265	-16.1462650824353	0.0466807612174442	-0.874007233794735	7.77066568488902E-16	BPG
ENSG00000128591	-41.7447306791569	0.033855976152254	-0.864883069086945	0.000120766630439194	BPG
ENSG00000165029	-22.8506787330317	0.0434195105580634	-0.86291825524471	0.000454633977955596	BPG
ENSG00000078018	-10.7717569786535	0.00396620119435979	-0.856913044052906	0.00025794820431816	BPG
ENSG00000146859	-21.2696586114308	0.020578924497702	-0.84633481531018	0.00169353470872061	BPG
ENSG00000135837	-13.4615384615385	0.0364112534338288	-0.841914617768189	4.39815806229496E-30	BPG
ENSG00000088002	-19.2363636363636	0.0244052415164296	-0.82505692379106	0.0298353550538748	BPG
ENSG00000134627	-19.2347990081375	0.00457463014138334	-0.822461814447813	0.00844870159173753	BPG
ENSG00000164506	-38.9090909090909	7.65818641689538E-06	-0.811913700700874	8.39113318714483E-09	BPG
ENSG00000174827	-13.8363659498664	0.0341624646108137	-0.807564997782899	6.86717565483119E-11	BPG
ENSG00000173145	-13.6073641997813	0.0496578294314864	-0.799516105316538	1.15159101940154E-05	BPG
ENSG00000164442	-10.0267379679144	0.0279776618927646	-0.795281537660393	6.31202055193831E-21	BPG
ENSG00000135925	-21.9082719082719	0.0254991791510193	-0.793619226035631	4.80751055745182E-06	BPG
ENSG00000066468	-10.2743271221532	0.0360674862820247	-0.79071950242535	7.93144139610672E-21	BPG
ENSG00000185352	-27.4216524216524	0.00144885499699453	-0.79007693062577	0.0447431224531728	BPG
ENSG00000049283	-12.5091575091575	0.0154280889548072	-0.788195343774151	0.00132370874713995	BPG
ENSG00000147883	-17.9003588416924	3.30391091025144E-05	-0.78473424255227	7.41560338748809E-22	BPG
ENSG00000186472	-11.34996582365	0.0305643480187316	-0.77420499444271	2.61961422751016E-06	BPG
ENSG00000073060	-25.6318407960199	0.0328814878548733	-0.772455864688409	1.76586173067377E-31	BPG
ENSG00000176809	-11.1764705882353	0.000514175858907286	-0.763084655130088	0.000800654523769907	BPG
ENSG00000063180	-21.0976523476523	0.0222779988761963	-0.755016874448972	0.00844328231083494	BPG
ENSG00000170477	-11.7304189435337	0.0269448063337879	-0.742503777707636	1.3230872226162E-08	BPG
ENSG00000132530	-28.827519379845	0.00370560489179961	-0.739203265142935	1.31129592238285E-06	BPG
ENSG00000253910	-11.9346222128117	0.0414994203111755	-0.72950014391964	0.0396713817830189	BPG
ENSG00000196872	-21.8078218078218	0.00380004619688595	-0.727960780904998	1.35353238986487E-09	BPG
ENSG00000126217	-35.85729339154	0.000935043160388676	-0.721570218766501	5.08518675875215E-07	BPG
ENSG00000165861	-11.4021931140219	0.00763535184916297	-0.720961014729347	7.00257301272694E-09	BPG
ENSG00000078804	-10.8225108225108	0.00928397592980438	-0.719263592432747	1.32150632916988E-06	BPG
ENSG00000196159	-14.8936170212766	0.0471818011006502	-0.717525713342523	1.86638251549598E-07	BPG
ENSG00000256223	-16.3728567978749	0.0174051731046039	-0.715820262853991	0.000393372988416042	BPG
ENSG00000120093	-25.3233687841334	1.01612381858311E-12	-0.714467624516055	0.0242160980884065	BPG
ENSG00000137261	-29.2911943203939	0.0306274405863407	-0.70626879694329	0.00736742878448766	BPG
ENSG00000113448	-23.7878787878788	0.0277146558900479	-0.705491592161748	4.54141174788106E-07	BPG
ENSG00000182580	-13.1755341432761	0.0401831561820508	-0.704544116473825	0.00558262764757869	BPG
ENSG00000154265	-11.7605910899313	0.000789266764691025	-0.704077083584603	1.45827370046656E-06	BPG
ENSG00000134030	-17.2413793103448	0.0440574659353242	-0.703735064599572	0.00423651266925635	BPG
ENSG00000153113	-12.8383413219479	0.00247776438292905	-0.703518178232066	1.42459864428974E-14	BPG
ENSG00000064787	-13.652989821883	0.0244339815607894	-0.696607856550066	4.6594488010428E-06	BPG
ENSG00000138764	-34.7946725860155	0.000333173550939385	-0.695928088181486	2.71937010624573E-14	BPG
ENSG00000188026	-14.1176470588235	0.0459663762263134	-0.694037324976346	0.023738157713412	BPG
ENSG00000196417	-22.0108950878182	0.0120084340558698	-0.690451059239939	0.00048897912138809	BPG
ENSG00000130635	-17.720207253886	0.0492072592643873	-0.685198409708279	1.26290044816402E-26	BPG
ENSG00000163071	-17.8918650793651	0.000238225772485735	-0.68326457433296	0.0160637005422413	BPG
ENSG00000162616	-10.1658977127712	0.00489225511347078	-0.677964365696175	4.80260658941897E-12	BPG
ENSG00000150347	-13.3711042556557	0.000279912881808571	-0.668489279530708	1.18874074373337E-26	BPG
ENSG00000239704	-49.5726495726496	0.00319349673251791	-0.667424660913131	0.0143437957934638	BPG
ENSG00000196227	-16.7942942942943	0.00329264008508148	-0.662382727403818	3.58986363598043E-10	BPG
ENSG00000146350	-20.1736542954448	3.35326970164892E-05	-0.653262229789643	0.00944152725963259	BPG
ENSG00000120784	-29.6452328159645	0.0186782132873125	-0.651513693629762	0.0146042259180537	BPG
ENSG00000186806	-26.4183561213264	0.00983045396353613	-0.649858302947994	0.00754359177228354	BPG
ENSG00000158321	-24.1720883887228	0.028801593296161	-0.648265082629678	0.00534070540002623	BPG
ENSG00000004399	-11.0782295419455	0.0466824666406132	-0.643196863834183	0.00186187396969658	BPG
ENSG00000167720	-14.0460174285277	0.0121783610214339	-0.638444830991933	0.00499040741340259	BPG
ENSG00000166473	-18.6415415735122	0.0140373551765548	-0.637980883020648	0.0350745435774593	BPG
ENSG00000161328	-16.1817226890756	0.0456827331161719	-0.626321530482211	0.0311368727613035	BPG
ENSG00000105357	-21.8991534781008	0.033635003674445	-0.620745655468585	2.7355022608927E-18	BPG
ENSG00000110975	-11.6666666666667	0.0378117878869766	-0.620411336725446	0.00614008621027657	BPG
ENSG00000121281	-31.036531036531	0.000108395658331335	-0.620078087582796	0.00134564043630872	BPG
ENSG00000198682	-12.2528100018032	0.000145080197988415	-0.618563904087295	1.88074343089455E-10	BPG
ENSG00000181035	-17.948717948718	1.1243993955062E-06	-0.613645255425247	0.00752603927024964	BPG
ENSG00000249437	-10.4472025216706	0.0191099409923715	-0.600838259722475	0.000312463160490006	BPG
ENSG00000119280	-22.9323308270677	0.00448911230662707	-0.598855003274603	4.87658245333588E-05	BPG
ENSG00000081189	-18.8919888401754	0.0458657425156468	-0.592175990953731	1.68981299065485E-05	BPG
ENSG00000142798	-21.5303215303215	0.0231716063266128	-0.5899034146544	8.21742467592223E-12	BPG
ENSG00000148180	-22.0766831773986	0.00333445198565143	-0.58507858029968	1.02616245712461E-21	BPG

(*continued on next page*)

Table 6 (*continued*)

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ENSG00000163406	-17.7479892761394	0.00255182037669778	-0.577405149543082	0.0121769142274754	BPG
ENSG00000152284	-18.9802631578947	0.0164930267945575	-0.573347871818441	0.00169316922396989	BPG
ENSG00000181555	-18.7059993878176	0.00642328434364566	-0.57045000701778	0.000633772036520459	BPG
ENSG00000132825	-16.7942942942943	0.00329264008508148	-0.567278581158528	3.64112288296977E-08	BPG
ENSG00000214960	-25	0.016295176120114	-0.566616208240501	0.000191551711513297	BPG
ENSG00000116117	-57.8347578347578	0.00293279455643258	-0.565110565625496	0.00619843887025926	BPG
ENSG00000179240	-21.3538363982245	0.0341784248396807	-0.562569888678666	0.000174515953525452	BPG
ENSG00000139173	-25.6965174129353	0.0437445774727228	-0.561479359762611	0.00409511772182182	BPG
ENSG00000185261	-20.0123757094696	0.020052417848434	-0.553253640993819	0.0362478930997127	BPG
ENSG00000020181	-12.7834293418311	0.032356879366654	-0.546427899302171	0.00983148706722227	BPG
ENSG00000114805	-19.3918531267929	0.0108898114101458	-0.543298174118273	0.00195123896760484	BPG
ENSG00000197050	-18.4495021337127	0.0198866741668744	-0.538866086131702	0.00624942651321243	BPG
ENSG00000184012	-18.1991879627418	0.00597710816950326	-0.534540606687861	2.80433524861581E-05	BPG
ENSG00000266074	-17.8296049500238	0.00673064892733957	-0.532013620772197	0.00290890178605587	BPG
ENSG00000137710	-17.024154589372	0.0194503531162814	-0.509881553601421	1.19794881274545E-11	BPG
ENSG00000286185	-25.5740107474353	0.0442468970760671	-0.508549385201989	0.0233281012293291	BPG
ENSG00000168952	-27.0041227668346	0.0361783351821684	-0.506001358375646	0.000757715658056192	BPG
ENSG00000065717	-19.2005157962605	0.0465447514310898	-0.505023206478345	0.030178121078624	BPG
ENSG00000128881	-14.7619047619048	0.0307063695905693	-0.503303250321294	0.000699512661491251	BPG
ENSG00000288611	-27.1107196097032	4.90113226319831E-12	-0.502383281415895	0.00136437218092605	BPG
ENSG00000197321	-14.9425287356322	0.0469346695243425	-0.501773106156611	5.87968999963141E-08	BPG
ENSG00000004468	-17.7096492080459	0.010110582357382	-0.498784546838366	2.88191330173453E-19	BPG
ENSG00000031003	-12.6666666666667	0.0165147742367946	-0.498416665958258	1.62058029177946E-05	BPG
ENSG00000185442	-32.776171924092	0.00749766036878492	-0.488240690456756	0.000221616026621544	BPG
ENSG00000010810	-13.6842105263158	0.0191245606116734	-0.486449571915371	0.000413551472221232	BPG
ENSG00000133056	-40.8445576993083	0.000905019819790039	-0.48630858030407	6.28258786955604E-06	BPG
ENSG00000111335	-11.1763191763192	0.0235768105093155	-0.485212793338396	4.18687964443166E-14	BPG
ENSG00000137941	-15.3955260171827	0.00014539576338224	-0.483014293094851	0.005048594733699	BPG
ENSG00000155621	-11.3020890206718	0.015856947109812	-0.47892536403238	0.00239940453361955	BPG
ENSG00000185630	-42.9711751662971	0.00600531248549614	-0.476626525138652	4.68402347442217E-06	BPG
ENSG00000166387	-21.7245146650979	0.0443533343534964	-0.475296219553436	0.0011843075479458	BPG
ENSG00000104687	-11.4678899082569	0.0348851228680506	-0.464375020256106	6.97868723476842E-05	BPG
ENSG00000182621	-14.1242265587815	0.0189228623228636	-0.460113840733944	0.00511236354729573	BPG
ENSG00000126016	-35.2063492063492	0.0276634704800075	-0.459114019287442	0.000389295435109945	BPG
ENSG00000107864	-28.9068825910931	0.0209329546065706	-0.458141001249102	0.0326818098866569	BPG
ENSG00000136295	-11.6443959640033	0.0323485301149538	-0.458073580642192	0.000508698691512146	BPG
ENSG00000165072	-19.0677025527192	0.000339771897715373	-0.45645563299263	1.97166067202811E-06	BPG
ENSG00000171604	-18.9543197074715	4.17294718598 55E-08	-0.453648847676855	1.39816502664685E-06	BPG
ENSG00000035862	-15.7889507154213	0.0468290151418606	-0.451158553185102	4.78852687458916E-18	BPG
ENSG00000151690	-14.4205594598319	0.0104011052091819	-0.449636871552875	0.000999885078613307	BPG
ENSG00000186350	-19.2988014150694	0.0017111929157375	-0.448057242810654	1.55132841468133E-14	BPG
ENSG00000129933	-15.0412087912088	0.0317264087153831	-0.444759038098622	0.0374773939660338	BPG
ENSG00000119771	-31.5789473684211	0.0321213640771322	-0.44461773449381	0.000411429515895675	BPG
ENSG00000118777	-22.9389788293898	0.000234720797535922	-0.442408470794975	6.46795535036693E-06	BPG
ENSG00000117114	-20	0.0261546286341399	-0.441252757186227	0.000523087175169761	BPG
ENSG00000135596	-24.2690058479532	0.0273177882292688	-0.439942841041666	0.00918029544146054	BPG
ENSG00000053254	-20.0134027120782	0.038465108119542	-0.439027674185821	1.53454946009585E-08	BPG
ENSG00000137642	-11.5808823529412	0.0216307609026432	-0.436013456287618	7.68304029801625E-11	BPG
ENSG00000004766	-11.4812063586391	0.0415076545920972	-0.435199538758269	0.0165862605250558	BPG
ENSG00000173269	-21.638418079096	0.0451104664416307	-0.434535907955739	0.00346600064214692	BPG
ENSG00000060656	-14.5128849780012	0.0235178287141165	-0.430759874289997	0.00126382471978609	BPG
ENSG00000024422	-26.7651080120317	8.74869238951487E-07	-0.430742625234609	0.0292165467312493	BPG
ENSG00000263001	-12.4821415143996	4.13774880745456E-05	-0.427605769403905	1.30049770019362E-15	BPG
ENSG00000174938	-31.3690169840453	0.00566139896404944	-0.427578762750185	0.00943681282532973	BPG
ENSG00000122042	-11.3924050632911	0.0453494958684685	-0.426135208162175	6.74272007444918E-06	BPG
ENSG00000159882	-11.1559109843844	0.00349377912991324	-0.423414847816786	0.0126593449204417	BPG
ENSG00000076067	-10.172441069451	0.0322621422851104	-0.422942697364189	0.000138197954281027	BPG
ENSG00000111110	-16.2162162162162	0.0427487766122153	-0.422821207581922	7.20801592208993E-13	BPG
ENSG00000119772	-23.7141148325359	0.0163957352760807	-0.421826664941483	1.21514223997701E-08	BPG
ENSG00000114904	-10.8284048255516	0.0241379586403085	-0.420381720055679	4.72687968962056E-06	BPG
ENSG00000213626	-20.530703202377	0.000146032484618759	-0.414439738739572	9.3078793953285E-09	BPG
ENSG00000107485	-27.8860569715142	0.0301130999882541	-0.413948336504497	1.75626784325988E-05	BPG
ENSG00000104447	-12.250554323725	0.0017224362480735	-0.411834331696803	1.05945304519687E-12	BPG
ENSG00000105289	-26.3516583371195	0.00243834530570209	-0.41174610474983	0.00268329936508764	BPG
ENSG00000196189	-19.8748299319728	0.0351914032748957	-0.411650094480343	0.000186204771936961	BPG
ENSG00000076554	-11.3150813486933	0.0464255898730151	-0.408729640831393	0.000156010695767343	BPG
ENSG00000184384	-16.7614498028511	0.0197342494549712	-0.40859384701675	1.90834843581944E-08	BPG
ENSG00000106799	-12	0.01330417194986	-0.407774072780301	0.000280359663905417	BPG
ENSG00000021826	-23.6842105263158	0.0462736889243597	-0.405337418500074	0.00616383842515306	BPG
ENSG00000005187	-17.038789025544	0.0153436175619191	-0.403418416012008	0.0448865535404382	BPG
ENSG00000133943	-14.8343361013044	0.00591261719440728	-0.403301391227878	0.000100742003170586	BPG
ENSG00000011028	-21.595015576324	0.0171678013900045	-0.402874720298177	9.42467032388253E-07	BPG
ENSG00000127663	-33.6503623188406	0.00171051555895984	-0.401869868853929	2.86929099910416E-05	BPG
ENSG00000141570	-11.2593052109181	0.0144163128036595	-0.400763699039544	0.00755259880380841	BPG

Table 6 (*continued*)

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ENSG00000275395	-26.265664160401	0.00777188474259746	-0.399832627667512	0.00313125281698433	BPG
ENSG00000103126	-21.3554987212276	0.000201394510843982	-0.398908443869134	1.94566970403727E-05	BPG
ENSG00000140836	-33.0721003134796	0.0420168370380255	-0.398451891606571	9.35526164448217E-08	BPG
ENSG00000118257	-23.2538713615627	0.00139916562865624	-0.398420727705338	0.000143402070040823	BPG
ENSG00000172493	-21.3652535729361	0.0372534055870424	-0.38972945200723	0.0234032173352906	BPG
ENSG00000090020	-19.2743288590604	0.015861808311544	-0.388856683389991	0.000518778442434831	BPG
ENSG00000053108	-34.5943673812526	0.0253805519864271	-0.387579503772093	0.0424531936840138	BPG
ENSG00000138759	-11.5113137944056	0.0337883711297745	-0.387473859671809	0.0257016002817308	BPG
ENSG00000140396	-10.8151549942595	0.0360233343840566	-0.386742552310836	0.000239083816398964	BPG
ENSG00000137145	-18.2248096730855	0.00508177320801475	-0.383559267805676	1.10343356270823E-08	BPG
ENSG00000033800	-10.8055262849783	3.62593955542093E-05	-0.38191478078331	4.91471783275079E-07	BPG
ENSG00000067208	-10.2189781021898	0.00498029617865129	-0.381634341011633	0.0143609651949742	BPG
ENSG00000149571	-35.1841820151679	0.0322340724629596	-0.38124062832878	0.00038268469644075	BPG
ENSG00000148411	-18.2267749911692	0.0311200040968892	-0.380991780541891	0.000130763088080944	BPG
ENSG00000166263	-22.2222222222222	0.00924873499321939	-0.380744321724967	0.000418729852976832	BPG
ENSG00000108370	-20.2324224448118	0.0224885565269278	-0.376513232652959	0.0357246871062311	BPG
ENSG00000177425	-30.9791332263242	0.0290104230584578	-0.374495972949755	0.00621084614505039	BPG
ENSG00000071909	-27.1900269541779	0.026966427274738	-0.373123857545449	0.0344094454284773	BPG
ENSG00000147852	-10.9904673331783	0.0499202989198112	-0.370732125655407	8.07912484025131E-06	BPG
ENSG00000213463	-18.4473929236499	0.000409714520048529	-0.369621388831842	0.0117890081504949	BPG
ENSG00000183111	-14.1414141414141	0.0234289623507625	-0.369058181807338	0.000887079686645829	BPG
ENSG00000103544	-15.7894736842105	0.0135107886884008	-0.368911930402233	0.00796346489599808	BPG
ENSG00000142065	-15.5963302752294	0.00642989573367869	-0.368867317845923	0.0061016352497874	BPG
ENSG00000000971	-18.6928104575163	0.0381543097810529	-0.368156784815649	0.00829744213311694	BPG
ENSG00000196498	-26.3157894736842	0.00716785210795178	-0.365364917610353	0.0024253152303974	BPG
ENSG00000167930	-25.9743954480797	0.0132126767562927	-0.364788396824613	0.000160436626026178	BPG
ENSG00000164463	-29.6296296296296	0.0116456414843442	-0.36011128877525	2.00051018268182E-08	BPG
ENSG00000149932	-22.6774193548387	0.0147586695726215	-0.359641098179801	0.00798093556666294	BPG
ENSG00000133121	-24.5989304812834	0.0362428273664653	-0.359284458342618	3.70422379108297E-06	BPG
ENSG00000163430	-26.4274497487437	2.06667236117478E-12	-0.357847922538527	4.99082827647821E-16	BPG
ENSG00000165813	-13.3241758241758	0.0234969527049207	-0.35652546997289	8.29764421380416E-05	BPG
ENSG00000048707	-27.2341597796143	0.00733359766974552	-0.355910194316597	0.00460082542307338	BPG
ENSG00000115419	-12.2636856814072	0.00233942838867749	-0.3534824267315	0.000700021903309769	BPG
ENSG00000168769	-11.8910939806462	0.00924277200859742	-0.352781048803786	0.000226578959147252	BPG
ENSG00000144036	-10.1010101010101	0.0415913214659878	-0.351100145352023	1.30393720844209E-07	BPG
ENSG00000090905	-10.5896368883818	0.0144273051946461	-0.347832227062783	0.000471463587356345	BPG
ENSG00000112983	-13.0574767469592	4.72308756925635E-06	-0.347495648150863	6.32052916426757E-05	BPG
ENSG00000035664	-12.7271804244086	0.0333961822126745	-0.347029855464279	0.000251558833382371	BPG
ENSG00000011347	-19.7648728083511	0.000716431069673398	-0.346753803485244	0.000132820027074002	BPG
ENSG00000145743	-12.4588744588745	0.0312074337643093	-0.345848057083885	0.00115791649628188	BPG
ENSG00000185621	-12.5049648435403	0.00644783960827106	-0.342887713523009	0.00947313600986688	BPG
ENSG00000054267	-10.4492959974688	0.025373302489601	-0.342210031447351	5.14097041637532E-05	BPG
ENSG00000078687	-15.5804849162746	0.0198389185083253	-0.341871086716868	0.00112924317517576	BPG
ENSG00000109618	-29.5842345590002	0.0300916586865236	-0.339962017717625	0.00326955308091664	BPG
ENSG00000126705	-26.0695011188627	4.62071581198193E-05	-0.336920809362834	3.74083405840874E-06	BPG
ENSG00000187498	-10.4905764966741	0.0192200266176312	-0.336870943565742	1.33866133734124E-06	BPG
ENSG00000078114	-32.7096774193548	0.0160013884423327	-0.336614795442298	3.31483817017941E-07	BPG
ENSG00000257923	-33.3935561577838	0.0140879640094156	-0.333068652492565	7.22255658121801E-05	BPG
ENSG00000118898	-24.1774151092393	1.67516345394496E-05	-0.332136872186805	1.43092872225816E-06	BPG
ENSG00000108840	-12	0.0125161345866882	-0.330166204586187	8.37847751568423E-06	BPG
ENSG00000090615	-25.3346855983773	5.86662883997356E-06	-0.326546834385105	0.00245668100546887	BPG
ENSG00000124788	-22.4137931034483	0.000301981434417419	-0.3247633955855	5.48725590404673E-18	BPG
ENSG00000169967	-11.4583333333333	0.0339287737679039	-0.324675795510129	2.87816468590847E-08	BPG
ENSG00000148400	-12.2994652406417	0.0327847423666243	-0.322624320288574	0.00334632511147991	BPG
ENSG00000168143	-20.8005249343832	0.0224423004027622	-0.321704369207935	0.000648834340912548	BPG
ENSG00000158828	-13.0841121495327	0.00836764608199518	-0.32169317290553	0.000252368264090229	BPG
ENSG00000091622	-10.3234914246238	0.0437409493308147	-0.319576087235189	0.0257875483845378	BPG
ENSG00000167755	-37.6623376623377	0.00152676786261716	-0.318421604149615	1.12887892117129E-06	BPG
ENSG00000196975	-10.4037267080745	0.0005631525966545	-0.318322994090514	0.000476234545672557	BPG
ENSG00000196935	-12.5095492742552	0.0312581984774442	-0.317212837258018	6.26141169093279E-06	BPG
ENSG00000105810	-17.3458725182863	0.0154453795157378	-0.316635644920549	0.000156775823491 7	BPG
ENSG00000179912	-10.8843537414966	0.00435216859219888	-0.315746578471056	0.000874410459462611	BPG
ENSG00000112144	-12.3076923076923	0.0352358160993718	-0.313903923802541	0.00138892875889279	BPG
ENSG00000196628	-26.4150943396226	0.00159773648008419	-0.313420129875148	3.28353137619013E-05	BPG
ENSG00000175155	-10.767405236335	0.0492552564194126	-0.313192706891764	0.00257815783289071	BPG
ENSG00000131149	-72.3484848484848	6.02086208344641E-07	-0.312479031368485	8.88086989224702E-05	BPG
ENSG00000173402	-17.3076923076923	0.00259101568638736	-0.311495771507253	6.72980902479292E-07	BPG
ENSG00000172817	-13.0865201372126	0.0148212401623412	-0.310860790984529	0.000193135720485011	BPG
ENSG00000033122	-15.1976099351714	0.0443638347308002	-0.306925931548116	0.00649183678214571	BPG
ENSG00000188064	-12.2101449275362	0.0219575344210156	-0.30632285680212	0.00403868260498254	BPG
ENSG00000145431	-11.3122820427077	0.0245549610355889	-0.304810542546114	0.0331405587117779	BPG
ENSG00000168795	-10.063648762746	0.035655980992928	-0.304780788272944	0.00124804558314024	BPG
ENSG00000152104	-19.5183486238532	0.0186903174950322	-0.304201627678951	9.3801020593915E-09	BPG
ENSG00000171517	-10.7142857142857	0.030254997250585	-0.303203453090096	0.027909916119053	BPG

(*continued on next page*)

Table 6 (*continued*)

id	meth.diff	meth.q	gene_fc	gene_p	
ENSG00000148498	-25.6010171058715	0.00121364071948905	-0.302775645054516	0.000599403897821241	BPG
ENSG00000109654	-37.5	0.0341617113401962	-0.301685799799022	0.0170642350636622	BPG
ENSG00000107104	-10.3243861338469	0.0431702429948203	-0.300742764996734	0.00633350140038271	BPG
ENSG00000130844	-39.983164983165	4.16525166325114E-10	-0.300668723482284	0.00719998180056289	BPG
ENSG00000217128	-11.6228070175439	0.0495363996427847	-0.298728320110066	9.04052804294962E-05	BPG
ENSG00000091157	-13.7931034482759	0.0109254916292158	-0.297059220774465	0.0374840228006454	BPG
ENSG00000144306	-17.2854441575341	0.00559347748568485	-0.293767533373402	0.0228695802793786	BPG
ENSG00000146648	-15.6407144095717	0.037114166441291	-0.293703786413115	2.29989877751664E-08	BPG
ENSG00000013288	-20.1121794871795	0.00270720181302578	-0.293473449710851	0.000421015976627107	BPG
ENSG00000075568	-21.9716494845361	0.0419162189190783	-0.293035982058586	0.0302709234446858	BPG
ENSG00000163701	-11.1111111111111	0.0356666493579973	-0.292553492753849	0.0388021610140557	BPG
ENSG00000105426	-19.0459067481721	0.0115227968479095	-0.29136312889229	9.61011029442332E-06	BPG
ENSG00000142784	-15.6462585034014	0.0170921943617	-0.291309926911496	0.000705471601159669	BPG
ENSG00000213694	-15.9353471118177	0.000600072464513817	-0.289866885655064	0.00708301690362163	BPG
ENSG00000119711	-20.3245942571785	0.00640464663479342	-0.289825497682747	0.0011433293486166	BPG
ENSG00000124587	-10.219068956933	0.0480419481129848	-0.289260874309599	0.0126463946039842	BPG
ENSG00000122779	-23.0899830220713	0.0338399491511729	-0.286905809452637	0.0312074493440943	BPG
ENSG00000133424	-29.8483736854977	0.00295502009273725	-0.285218427692496	0.0188359404674102	BPG
ENSG00000164073	-15.3201571890892	0.0150902906467985	-0.283527577697872	0.0348579282153239	BPG
ENSG00000196743	-15.7559198542805	0.00253350944854052	-0.28258280221177	0.00252542188050536	BPG
ENSG00000133983	-18.4473929236499	0.000409714520048529	-0.28200331050987	0.0264347269628561	BPG
ENSG00000137802	-29.5496991076987	0.045919863933346	-0.279574081983723	6.17422330703431E-07	BPG
ENSG00000177426	-16.8514136992784	0.0019906890357851	-0.279003057669837	4.43854792534203E-05	BPG
ENSG00000139266	-26.486915146709	2.18453721103963E-13	-0.277918279325949	0.0404238161915395	BPG
ENSG00000183018	-15.8710730314158	0.0303798945817675	-0.275184263619617	0.0380516157947918	BPG
ENSG00000125637	-19.8146513680494	0.0255341249935498	-0.272566168006445	0.0497067351784928	BPG
ENSG00000197757	-11.0945824396319	0.0237079682771938	-0.271302021817394	0.0131892309227297	BPG
ENSG00000177853	-11.0696612105063	0.00840131928524951	-0.268605858957599	0.0290459942156785	BPG
ENSG00000054965	-15	0.0466784626955542	-0.267963637356679	0.000293100155619997	BPG
ENSG00000148842	-11.4588050599281	0.0266352962539337	-0.267695783203657	0.00377595052802898	BPG
ENSG00000123636	-28.1315458734814	0.0140819601108139	-0.267416852462943	0.011351823485927	BPG
ENSG00000126858	-12.2970639032815	0.000516604023102541	-0.266499681624815	0.0311298311886331	BPG
ENSG00000162434	-20	0.033302838632579	-0.263612329451374	4.94379178207903E-08	BPG
ENSG00000243708	11.4285714285714	0.0459755722858929	-10.2086408085582	0.0303914223244126	BNG
ENSG00000285791	11.6889326831308	2.58663260106533E-05	-5.32192809488736	0.0444464233284871	BNG
ENSG00000284686	15.2453424298085	0.0142705765108504	-4.56478461878353	0.0159534725530422	BNG
ENSG00000284554	20.4896907216495	0.0239166953197774	-2.88452278258007	0.0161004908719089	BNG
ENSG00000141052	23.4808612440191	0.0332321208951147	-2.84130225398094	0.00445823481164802	BNG
ENSG00000198673	34.2760180995475	0.0471210718080951	-2.67807190511264	0.0262071277264242	BNG
ENSG00000166509	23.8829833203699	0.000107100204342874	-2.44166733916145	9.2409671837753E-10	BNG
ENSG00000172346	13.8792102206736	0.0338485749067207	-2.30666133823405	0.00785735661929826	BNG
ENSG00000055163	18.4180790960452	0.0478510307688422	-2.2829339632715	0.0165454370593668	BNG
ENSG00000144218	26.7397628104721	0.0231025020147638	-2.17791779219585	1.12979214761745E-05	BNG
ENSG00000085741	21.8053804119378	0.0099531998749705	-1.96578428466209	0.000496517358048221	BNG
ENSG00000122367	14.6890216261722	0.000179835622794449	-1.85561009066482	0.00523883401102577	BNG
ENSG00000159450	11.9856933865753	0.0244013429886495	-1.85414913353655	0.00369912599429018	BNG
ENSG00000170871	20.7547169811321	0.0356584465615654	-1.66699826958717	4.56446949371295E-10	BNG
ENSG00000145526	27.8409090909091	0.0265871205051091	-1.61598939634178	0.00646044956681184	BNG
ENSG00000184588	21.6815809097688	0.0320487792308055	-1.6000299488101	3.46814360898919E-07	BNG
ENSG00000177679	27.6068965517241	0.0141703113104466	-1.59991284218712	0.0138522073197324	BNG
ENSG00000115844	19.5057536313903	0.023166417767195	-1.4723706743448	0.00193013004584154	BNG
ENSG00000134516	22.2453646981949	0.0240135392868345	-1.41503749927884	0.018051969347599	BNG
ENSG00000137834	11.8944143630664	0.0161432184490245	-1.4039992278264	1.34050871745801E-05	BNG
ENSG00000164292	19.9233716475096	0.0364557999486495	-1.32775695358668	2.06829375217998E-43	BNG
ENSG00000110693	20.5844828001252	0.0214335484821773	-1.3112016882943	0.00661793779747204	BNG
ENSG00000031081	11.8811881188119	0.0285139918378	-1.30618535834161	0.0136161269955364	BNG
ENSG00000104081	14.6915584415584	0.0266766311662972	-1.28504761764604	2.89295613727264E-29	BNG
ENSG00000179869	14.2641077523658	0.036012662655069	-1.27077305420077	2.96061122587694E-26	BNG
ENSG00000183307	32.9376854599407	7.37254582691034E-06	-1.25779775746765	0.0201283284961805	BNG
ENSG00000125378	23.908804559772	0.0141634247950583	-1.22239242133645	0.00421868324091519	BNG
ENSG00000187720	13.1598457888494	8.52728379619754E-05	-1.13814629276965	0.012520318473065	BNG
ENSG00000143341	17.9016221873365	0.0235758336459982	-1.13670923392942	6.97523100767761E-36	BNG
ENSG00000112902	27.8081467113384	0.0190729888469772	-1.11393198503502	1.05408010797426E-37	BNG
ENSG00000050628	29.1620207564971	0.0142390504680928	-1.11103131238874	0.0159352652065548	BNG
ENSG00000164125	11.1111111111111	0.0114068205386867	-1.0994888016056	2.13172674056113E-29	BNG
ENSG00000172348	35.0877192982456	0.0256081938719352	-1.09019780897158	0.0423127348056044	BNG
ENSG00000166147	36.1985472154964	0.0302694806912422	-1.07480383893417	5.03157126804725E-30	BNG
ENSG00000168477	24.7942386831276	0.000309416960514426	-1.07297944535711	4.18654241470581E-09	BNG
ENSG00000227051	19.4767441860465	0.00156131261208117	-1.06558834162758	0.0116318181984038	BNG
ENSG00000204947	10.9382151029748	0.0400885775398988	-1.05794734920928	0.00408853581326887	BNG
ENSG00000178026	29.3280632411067	0.0436981213068628	-1.03963178689293	0.0125500731349175	BNG
ENSG00000130701	12.666383460776	0.0374981214266512	-1.03652587602511	0.00215566552074285	BNG
ENSG00000069702	13.8827838827839	0.0270751116053932	-1.02537178970831	1.85966982990304E-10	BNG
ENSG00000168916	13.0047371982856	0.00666888599889314	-1.02291693739155	0.0298227184961054	BNG
ENSG00000116039	21.7977019301523	0.0182959230355484	-1.01495034146597	0.00147837289196474	BNG

Table 6 (*continued*)

id	meth.diff	meth.q	gene_fc	gene_p	
ENSG00000157502	10.7212071629852	0.0298875776396145	-0.99885817561045	1.63962018298735E-17	BNG
ENSG00000097096	11.0371346956713	0.0175081999482966	-0.996406735275991	1.53173247911141E-18	BNG
ENSG00000197183	15.8699862994284	0.0248089139195588	-0.987198717776908	0.0149582145196133	BNG
ENSG00000204103	12.66446797431	0.000520207556120523	-0.979535897440284	0.0445563180502833	BNG
ENSG00000182263	13.5664335664336	0.0044007150689271	-0.97480591784075	3.43643082167393E-14	BNG
ENSG00000111799	16.685280321644	0.0328568094477351	-0.951255666148583	1.60507703090466E-13	BNG
ENSG00000146477	18.4911717495987	0.0194503531162814	-0.936947829464703	0.000353422946928915	BNG
ENSG00000177076	15.863840719332	0.0144405638821234	-0.929610672108602	3.49843978402604E-12	BNG
ENSG00000126803	10.5054798516481	0.00219758317404919	-0.927718158319253	1.22276845523072E-24	BNG
ENSG00000114166	17.0500560006892	0.0188813032991278	-0.926874802389804	2.55900871212831E-07	BNG
ENSG00000167183	13.1452244989363	0.0112001369917942	-0.921163842447899	1.5003407140692E-08	BNG
ENSG00000185432	13.8783109080139	0.04153131178274	-0.918437760189343	1.3451990699202E-10	BNG
ENSG00000178568	37.0017128620367	2.62446043121715E-21	-0.888968687611259	0.0032937298473144	BNG
ENSG00000151623	11.9830450223393	0.0156272601196254	-0.888830624063527	2.85802238792563E-05	BNG
ENSG00000245848	28.8480263650663	0.000588322424264537	-0.882292014433902	1.19753165707245E-06	BNG
ENSG00000150893	12.7647612756328	0.0193133285667364	-0.867784804610925	2.03480136814508E-10	BNG
ENSG00000165029	15.7516412595972	0.0429688266413051	-0.86291825524471	0.000454633977955596	BNG
ENSG00000078018	18.6377708978328	0.0267348110796337	-0.856913044052906	0.00025794820431816	BNG
ENSG00000087085	20.9770114942529	0.0099341108704103	-0.841770332190061	0.000518237003680987	BNG
ENSG00000104205	10.0578466131741	8.69490707846433E-06	-0.837798814548365	1.07967548935029E-05	BNG
ENSG00000088002	41.5165165165165	0.0104801422938026	-0.82505692379106	0.0298353550538748	BNG
ENSG00000185924	11.3515115589804	0.0318484916420642	-0.797562185039193	0.000271873678644402	BNG
ENSG00000066468	31.0344827586207	0.00473328658620488	-0.79071950242535	7.93144139610672E-21	BNG
ENSG00000185352	15.4640921409214	0.0361105332861815	-0.79007693062577	0.0447431224531728	BNG
ENSG00000125848	14.0999692559951	0.0314930098693842	-0.786090105274825	0.0237497881247026	BNG
ENSG00000168453	16.1601597160603	0.0167552169351298	-0.752291325395042	0.00224328328413343	BNG
ENSG00000011201	34.5980126467931	0.040528242942424	-0.750374039136391	5.83095093384214E-05	BNG
ENSG00000176182	16.4007826021522	0.00102380692089381	-0.741364058063724	0.0382622065004552	BNG
ENSG00000139998	13.5398054397459	0.0302652271862405	-0.73884967913656	3.44175359709653E-16	BNG
ENSG00000253910	16.2661776264082	0.00844151005684433	-0.72950014391964	0.0396713817830189	BNG
ENSG00000196872	12.6008851861494	0.0459907985460533	-0.727960780904998	1.35353238986487E-09	BNG
ENSG00000126217	18.4417245158933	0.0478245948927844	-0.721570218766501	5.08518675875215E-07	BNG
ENSG00000165861	17.776590937102	2.8745872305254E-07	-0.720961014729347	7.00257301272694E-09	BNG
ENSG00000256223	18.1818181818182	0.0247394474772389	-0.715820262853991	0.000393372988416042	BNG
ENSG00000120093	14.7095375722543	0.0307865686470777	-0.714467624516055	0.0242160980884065	BNG
ENSG00000108984	17.728667038483	0.00475059817701297	-0.710175082739545	5.01107261444136E-23	BNG
ENSG00000137261	23.0116648992577	0.0417311399068192	-0.70626879694329	0.00736742878448766	BNG
ENSG00000113448	38.8888888888889	0.0445643717437885	-0.705491592161748	4.54141174788106E-07	BNG
ENSG00000143126	16.9444444444444	0.0291129750811605	-0.704692138332153	2.74246450392245E-05	BNG
ENSG00000134030	12.3072875559063	0.000780194592826204	-0.703735064599572	0.00423651266925635	BNG
ENSG00000153113	21.9307394036636	0.00374511905818774	-0.703518178232066	1.42459864428974E-14	BNG
ENSG00000179348	24.1163561656628	6.70182429095373E-08	-0.699514617089266	1.00020068482785E-07	BNG
ENSG00000064787	15.4477430029768	0.019433423253655	-0.696607856550066	4.6594488010428E-06	BNG
ENSG00000188026	36.2956810631229	0.0129326007149464	-0.694037324976346	0.023738157713412	BNG
ENSG00000221890	18.7572590011614	0.0308096453721258	-0.690795412733281	0.0176007089136136	BNG
ENSG00000196417	11.4957264957265	0.0125211169053565	-0.690451059239939	0.00048897912138809	BNG
ENSG00000130635	26.9356597600872	0.0271574565142418	-0.685198409708279	1.26290044816402E-26	BNG
ENSG00000111913	30.7936507936508	0.0414896056053475	-0.670840335881557	0.000101763314920898	BNG
ENSG00000150347	14.9859943977591	0.0440225685517479	-0.668489279530708	1.18874074373337E-26	BNG
ENSG00000116711	14.0571532580997	0.0297904753033027	-0.667339028324238	0.0283734297613091	BNG
ENSG00000196227	12.1661315424197	0.0106092170610959	-0.662382727403818	3.58986363598043E-10	BNG
ENSG00000002016	14.5918688937914	0.00312863804951235	-0.655096958010198	0.00272596416552348	BNG
ENSG00000146350	23.3137254901961	0.0146677698628851	-0.653262229789643	0.00944152725963259	BNG
ENSG00000145536	17.1686274509804	0.0427584023858685	-0.64965904943743	2.45479952909829E-05	BNG
ENSG00000158321	27.5966018087147	0.0101861074494865	-0.648265082629678	0.00534070540002623	BNG
ENSG00000171219	12.258064516129	0.00894773991707233	-0.643572286500509	4.99326325232002E-17	BNG
ENSG00000004399	15.4077540106952	0.0417624266596511	-0.643196863834183	0.00186187396969658	BNG
ENSG00000166473	41.9574468085106	0.0183894814151029	-0.637980883020648	0.0350745435774593	BNG
ENSG00000066382	14.5661819919448	0.0154570820713063	-0.63786558271762	0.00347335684687682	BNG
ENSG00000165124	11.3423575860124	0.0380101767330406	-0.63523570720238	0.000592958316482939	BNG
ENSG00000223573	29.0424725656918	6.20881894139791E-09	-0.630849959762384	2.28917372212143E-09	BNG
ENSG00000105357	11.5917067463928	0.0014517892392665	-0.620745655468585	2.7355022608927E-18	BNG
ENSG00000110975	16.7147730254526	0.00872311460033196	-0.620411336725446	0.00614008621027657	BNG
ENSG00000121281	13.0323989807062	0.0342477469741301	-0.620078087582796	0.00134564043630872	BNG
ENSG00000198682	10.4387656702025	0.00204118703000595	-0.618563904087295	1.88074343089455E-10	BNG
ENSG00000188153	11.5046244078502	0.025660119822895	-0.616462780545589	5.88521426071701E-15	BNG
ENSG00000181035	22.9144289294665	0.0147254762161582	-0.613645255425247	0.00752603927024964	BNG
ENSG00000005469	10.3174603174603	0.000499992831155057	-0.609148687022231	3.42678393928905E-06	BNG
ENSG00000075461	15.342989017985	0.00304300349665309	-0.605155649192202	2.28866368636362E-12	BNG
ENSG00000167861	11.7043294290795	0.00136830639884553	-0.600339911716719	1.51057836248098E-06	BNG
ENSG00000104936	10.3047080299292	0.0360010218041492	-0.597332951997686	4.00855123499364E-10	BNG
ENSG00000198691	22.6515151515152	0.0493777709424798	-0.587156714134073	0.000809594934608358	BNG
ENSG00000138336	16.9651741293532	0.0482494140512625	-0.587007426706185	0.000973023962220727	BNG
ENSG00000148180	23.2778604949207	3.57611619264839E-09	-0.58507858029968	1.02616245712461E-21	BNG

(*continued on next page*)

Table 6 (*continued*)

id	meth.diff	meth.q	gene_fc	gene_p	
ENSG00000164309	18.1738618461881	0.00164648726654438	-0.584962500721158	0.0173490350620861	BNG
ENSG00000165434	12.3711340206186	0.0445444711611503	-0.584708169289755	1.25825478046189E-10	BNG
ENSG00000198846	21.2872559095581	0.0153427691333421	-0.578938713093386	0.00289858288076006	BNG
ENSG00000152284	10.675049351987	0.0459654025511792	-0.573347871818441	0.00169316922396989	BNG
ENSG00000181555	20.5492050978846	0.00757578203996778	-0.57045000701778	0.000633772036520459	BNG
ENSG00000139973	19.6004700352526	0.0305810605288159	-0.570187148040758	0.00480345245979799	BNG
ENSG00000147912	12.7404413500118	0.00303259312325178	-0.569771393690503	0.00602492513846353	BNG
ENSG00000214960	14.1791044776119	0.000599946846525298	-0.566616208240501	0.000191551711513297	BNG
ENSG00000243317	32.6256043725037	0.0311519672052956	-0.56636438224004	0.0104549849382166	BNG
ENSG00000116117	25.4728492983526	0.000960434321705651	-0.565110565625496	0.00619843887025926	BNG
ENSG00000090238	15.1902643933778	0.0213139948134366	-0.556120748810073	0.0493146928859833	BNG
ENSG00000185261	31.9214131218457	0.0314674697603723	-0.553253640993819	0.0362478930997127	BNG
ENSG00000020181	12.4230657780354	0.001966428225144	-0.546427899302171	0.00983148706722227	BNG
ENSG00000128567	18.8532110091743	0.0182896877761265	-0.544534074812149	0.000147772976409115	BNG
ENSG00000120925	12.5353906074451	0.0196933918755241	-0.539247164748559	0.000736410991429054	BNG
ENSG00000197050	18.374307233196	0.000119040562611568	-0.538866086131702	0.00624942651321243	BNG
ENSG00000114423	23.9495798319328	0.0431958123249209	-0.535465534932059	1.7576048201707E-08	BNG
ENSG00000134321	13.6886005560704	0.00997575625153228	-0.522870156352437	7.04810893304969E-05	BNG
ENSG00000241489	24.2486554887694	0.00550099733479635	-0.522263595350611	0.00027164275856533	BNG
ENSG00000137070	12.0733953849137	0.0318905841876695	-0.521952703195358	0.0424631435708416	BNG
ENSG00000166689	24.5501775807919	0.00388073994598053	-0.516848119489151	1.81992158020414E-08	BNG
ENSG00000119686	14.484126984127	0.0332429167482642	-0.51377490313628	0.00213204060595649	BNG
ENSG00000137710	28.6331500392773	0.0389255987511811	-0.509881553601421	1.19794881274545E-11	BNG
ENSG00000128881	14.2607313195549	0.0119137103769155	-0.503303250321294	0.000699512661491251	BNG
ENSG00000127955	41.9444444444444	0.0354275939892162	-0.503216922792406	8.94381266527608E-08	BNG
ENSG00000197321	21.9171814230153	0.036646900840191	-0.501773106156611	5.87968999963141E-08	BNG
ENSG00000268043	22.653156300955	0.00400317217342186	-0.501256784016834	0.0182883160391524	BNG
ENSG00000107099	39.5915678524374	0.0195055406073874	-0.499845887083205	0.00208375996312581	BNG
ENSG00000004468	12.1951219512195	0.038467462223309	-0.498784546838366	2.88191330173453E-19	BNG
ENSG00000083123	22.5	0.0245859854332828	-0.498464583649882	0.000340419237867412	BNG
ENSG00000031003	26.6564318034906	0.0217127474516512	-0.498416665958258	1.62058029177946E-05	BNG
ENSG00000183044	17.5899742930591	0.000384657817382759	-0.497226809344069	8.54488863773884E-05	BNG
ENSG00000124467	23.8176470588235	0.0417943093826968	-0.495318902553343	0.00473377315997699	BNG
ENSG00000177303	25.5813953488372	0.0360479555471996	-0.491974622256619	8.7489021015237E-06	BNG
ENSG00000111961	26.078431372549	0.0407504283176384	-0.491236856643731	2.48976492107798E-14	BNG
ENSG00000185442	23.3378317588844	0.00174367822635544	-0.488240690456756	0.000221616026621544	BNG
ENSG00000010810	14.9159663865546	0.0425652235144658	-0.486449571915371	0.000413551472221232	BNG
ENSG00000111335	19.5384615384615	0.0471474911149716	-0.485212793338396	4.18687964443166E-14	BNG
ENSG00000114770	13.9481413009138	0.028967058065351	-0.484076384162012	4.02271054341108E-08	BNG
ENSG00000137941	11.8190079877553	0.0193456625379411	-0.483014293094851	0.005048594733699	BNG
ENSG00000149260	43.8095238095238	0.0222437844825907	-0.47822513286538	0.0144181754674735	BNG
ENSG00000105492	15.9129901960784	0.0318828061877183	-0.478047296804645	0.00855673971982164	BNG
ENSG00000072858	25.8367856908003	0.0271064512377889	-0.47669201719264	0.0434660969166838	BNG
ENSG00000185630	15.2542372881356	0.0443172927303969	-0.476626525138652	4.68402347442217E-06	BNG
ENSG00000166387	17.7108639863131	0.0295489808875449	-0.475296219553436	0.0011843075479458	BNG
ENSG00000124942	24.7691201681137	0.00103131086256605	-0.474392536230519	3.09603368050903E-14	BNG
ENSG00000008323	37.6282649253731	2.50661784039429E-14	-0.466707226346571	0.00140380214213413	BNG
ENSG00000138303	11.7647058823529	0.00199813755820777	-0.462618563812952	0.000191896181673512	BNG
ENSG00000125266	16.3265306122449	0.0460499274278431	-0.462355578124758	2.7748334758846E-16	BNG
ENSG00000182621	13.279334858637	0.0225777427225306	-0.460113840733944	0.00511236354729573	BNG
ENSG00000126016	16.5492777379367	0.00849881594750249	-0.459114019287442	0.000389295435109945	BNG
ENSG00000107864	12.2122403144301	0.0301314363561356	-0.458141001249102	0.0326818098866569	BNG
ENSG00000136295	13.7074829931973	0.000491213772379682	-0.458073580642192	0.000508698691512146	BNG
ENSG00000171604	27.7815405455329	0.00294096172983806	-0.453648847676855	1.39816502664685E-06	BNG
ENSG00000150556	37.5	0.0109836286899308	-0.453179487183903	0.00172366138067641	BNG
ENSG00000035862	18.5524520315241	0.0351743704365662	-0.451158553185102	4.78852687458916E-18	BNG
ENSG00000137414	10.5544440485652	0.00423248406173437	-0.447689697432434	4.30843512142587E-05	BNG
ENSG00000174456	14.3014604574263	0.0149410499960918	-0.44752315950708	0.03598620057456	BNG
ENSG00000129493	11.0504201680672	0.0144470729314065	-0.446655711835727	0.00778447877637807	BNG
ENSG00000196967	16.2420841567734	0.00025867693432669	-0.445467129297523	0.000224181365577937	BNG
ENSG00000129933	14.3144922384169	0.000432568102183404	-0.444759038098622	0.0374773939660338	BNG
ENSG00000119771	17.2413793103448	0.0388262077612964	-0.44461773449381	0.000411429515895675	BNG
ENSG00000121989	15.3653095370887	0.0302234057665656	-0.444528795988244	1.64215148130686E-05	BNG
ENSG00000118777	19.0268065268065	0.00898381918638679	-0.442408470794975	6.46795535036693E-06	BNG
ENSG00000117114	21.8518518518519	0.0258821518569486	-0.441252757186227	0.000523087175169761	BNG
ENSG00000170365	12.5051419169066	0.00956966372760876	-0.43934074696144	0.00396074346888895	BNG
ENSG00000053254	27.9874213836478	0.040395061954745	-0.439027674185821	1.53454946009585E-08	BNG
ENSG00000115616	12.036010811021	0.0492387190359769	-0.436445306227521	0.000115162802536429	BNG
ENSG00000177694	23.8667282714718	0.00987326807617852	-0.431558175834021	1.29491578718345E-09	BNG
ENSG00000024422	27.6158623984711	0.0168033859609324	-0.430742625234609	0.0292165467312493	BNG
ENSG00000263001	12.9596402622718	0.0185269299019678	-0.427605769403905	1.30049770019362E-15	BNG
ENSG00000104497	10.2733785822021	0.00730893312706585	-0.424642558756677	0.0219969817122393	BNG
ENSG00000076067	10.9556397409263	0.0059602672720826	-0.422942697364189	0.000138197954281027	BNG
ENSG00000111110	16.977466977467	0.000540722238095916	-0.422821207581922	7.20801592208993E-13	BNG
ENSG00000213626	29.9457994579946	0.0377276764664726	-0.414439738739572	9.3078793953285E-09	BNG

Table 6 (*continued*)

id	meth.diff	meth.q	gene_fc	gene_p	
ENSG00000172667	23.7246963562753	0.0474848655744828	-0.412851266035975	0.00143250843933229	BNG
ENSG00000105289	15.5648592072388	0.0110678259799135	-0.41174610474983	0.00268329936508764	BNG
ENSG00000135643	14.565610429156	0.0489006771605987	-0.410376121908981	0.0023753800622474	BNG
ENSG00000160325	12.0906136052402	0.0447524194044426	-0.410122008864727	0.0327554626240886	BNG
ENSG00000115904	15.9753456605031	0.00622289236958857	-0.409262861652211	2.21354668124224E-06	BNG
ENSG00000198551	25.9259259259259	0.0263223587684373	-0.408793558121986	0.0144574112408487	BNG
ENSG00000099139	17.3040667923512	0.0260782817068225	-0.408740260817638	2.0345655513523E-11	BNG
ENSG00000076554	30.1587301587302	0.026989458289609	-0.408729640831393	0.000156010695767343	BNG
ENSG00000184384	34.2731829573935	0.0457754145078931	-0.40859384701675	1.90834843581944E-08	BNG
ENSG00000152409	13.0952380952381	0.0089475018307773	-0.406334623724234	1.81980304651701E-06	BNG
ENSG00000185115	14.1691106321331	0.0486297174163698	-0.406285025269877	0.0471767784504365	BNG
ENSG00000133943	17.6787148594378	0.0024986162549337	-0.403301391227878	0.000100742003170586	BNG
ENSG00000011028	23.8768638768639	2.49177149563819E-08	-0.402874720298177	9.42467032388253E-07	BNG
ENSG00000127663	16.3120567375887	0.00199479787932435	-0.401869868853929	2.86929099910416E-05	BNG
ENSG00000275395	40.1215805471125	0.0161209738470805	-0.399832627667512	0.00313125281698433	BNG
ENSG00000140836	22.0262096774194	0.01353803363207	-0.398451891606571	9.35526164448217E-08	BNG
ENSG00000197121	13.3465608465608	0.000216837614926441	-0.398127720768761	6.40513117712682E-05	BNG
ENSG00000147394	14.7713025567546	1.37389673771049E-05	-0.393895478184056	0.00012655160829566	BNG
ENSG00000198624	15.3837342497136	0.0312565681270824	-0.391493449347894	0.019092758640645	BNG
ENSG00000172493	24.3243243243243	0.0326834339365618	-0.38972945200723	0.0234032173352906	BNG
ENSG00000090020	16.4556962025316	0.0416009438220768	-0.388856683389991	0.000518778442434831	BNG
ENSG00000112079	10.1827411167513	0.0100171189668929	-0.388199801705896	1.09379010875715E-07	BNG
ENSG00000138759	36	0.04992950805686	-0.387473859671809	0.0257016002817308	BNG
ENSG00000109323	12.2641509433962	0.0069510470048547	-0.386464027629376	0.00155007758709338	BNG
ENSG00000124006	19.0433862433862	0.0322288314190479	-0.386068098767428	1.87116592734966E-06	BNG
ENSG00000140044	10.7904578132204	9.33890316296523E-09	-0.381947673579412	0.0233492939076747	BNG
ENSG00000067208	10.6948341310447	0.0370695915488687	-0.381634341011633	0.0143609651949742	BNG
ENSG00000149571	15.7046791818436	0.0421796299620546	-0.38124062832878	0.00038268469644075	BNG
ENSG00000166263	15.625	0.00714785082935721	-0.380744321724967	0.000418729852976832	BNG
ENSG00000074621	37.2177055103884	0.0430195524117608	-0.376969458445324	0.0400580722604868	BNG
ENSG00000008300	24.3827160493827	0.00848287737033332	-0.376563351464209	0.0234887642424702	BNG
ENSG00000108370	17.6969178082192	0.000780062895708609	-0.376513232652959	0.0357246871062311	BNG
ENSG00000071909	12.0548116240597	0.0490054769874261	-0.373123857545449	0.0344094454284773	BNG
ENSG00000064655	16.4221364221364	0.018160735094327	-0.370785409945289	0.000286216813915154	BNG
ENSG00000147852	15.3964923393642	0.0338694660141525	-0.370732125655407	8.07912484025131E-06	BNG
ENSG00000103544	44.0711462450593	0.0137093219337725	-0.368911930402233	0.00796346489599808	BNG
ENSG00000142065	21.0619133402863	0.00758559471411506	-0.368867317845923	0.0061016352497874	BNG
ENSG00000166295	22.4340175953079	0.00231052665483842	-0.36854278853606	0.00529971793428787	BNG
ENSG00000196498	27.3656480505796	0.00165568906695835	-0.365364917610353	0.0024253152303974	BNG
ENSG00000107105	12.0634920634921	0.0487293089605174	-0.365260396902254	0.00142528327132613	BNG
ENSG00000110628	11.7507099547164	0.00605011299301495	-0.364197318260097	0.0233052964014367	BNG
ENSG00000145246	10.9188034188034	0.0460646211045671	-0.36064904708903	0.0135260007232632	BNG
ENSG00000164463	17.8451178451178	0.0115418200671948	-0.36011128877525	2.00051018268182E-08	BNG
ENSG00000197852	16.42166344294	0.0328002414526065	-0.358070903678058	0.0463281393522118	BNG
ENSG00000165813	16.8224299065421	0.00315028103681137	-0.35652546997289	8.29764421380416E-05	BNG
ENSG00000048707	14.821083172147	0.0443046839021289	-0.355910194316597	0.00460082542307338	BNG
ENSG00000146411	12.3137254901961	0.0111360967257588	-0.353548977358163	0.000126067031609596	BNG
ENSG00000110987	30.0347222222222	0.0421845647585318	-0.353265409587902	0.000559485941448659	BNG
ENSG00000111271	10.6666666666667	0.008468668423606	-0.353001616041892	0.00560907003355677	BNG
ENSG00000173960	16.7713039566587	0.0483843564132747	-0.352925140306958	0.0394304539177195	BNG
ENSG00000168769	12.5748502994012	0.000650725986752801	-0.352781048803786	0.000226578959147252	BNG
ENSG00000130702	11.1639672292068	0.0372983683188233	-0.35203751427251	2.20623970839814E-08	BNG
ENSG00000183354	12.8326330532213	0.0355388940157917	-0.351864288021866	0.0148775505018936	BNG
ENSG00000166025	11.875	0.00620759228648224	-0.34809950931572	1.15937311348668E-16	BNG
ENSG00000090905	33.4425155584671	0.0422728274876238	-0.347832227062783	0.000471463587356345	BNG
ENSG00000149639	18.4732335027705	0.0195307265727982	-0.347636760659084	0.00218329338042741	BNG
ENSG00000035664	43.3962264150943	0.000533581462920669	-0.347029855464279	0.000251558833382371	BNG
ENSG00000145743	11.3872941770235	0.0352501512573267	-0.345848057083885	0.00115791649628188	BNG
ENSG00000075651	12.3397435897436	0.0465276148281672	-0.345786234742914	1.02844545122384E-06	BNG
ENSG00000173230	10.5312229614822	0.0101047746531274	-0.344274253793976	4.53886715903854E-06	BNG
ENSG00000054267	10.2189781021898	0.0141196697095234	-0.342210031447351	5.14097041637532E-05	BNG
ENSG00000115464	11.1111111111111	0.00133219128075895	-0.340616368337588	0.00164951387603357	BNG
ENSG00000109618	33.179167665149	8.41930404674389E-16	-0.339962017717625	0.00326955308091664	BNG
ENSG00000108389	10.154017148301	0.00553242265274357	-0.33699162338449	0.000125906890521743	BNG
ENSG00000187498	11.733746130031	0.0385511399220718	-0.336870943565742	1.33866133734124E-06	BNG
ENSG00000078114	21.1104684788895	0.0469928272245415	-0.336614795442298	3.31483817017941E-07	BNG
ENSG00000134326	10.0901813475147	0.00955467281308764	-0.335910517196568	0.00768797119644126	BNG
ENSG00000176438	10.1892605633803	0.0159761741102653	-0.334560161543612	0.000737954103415541	BNG
ENSG00000257923	19.1239316239316	1.45731709371131E-05	-0.333068652492565	7.22255658121801E-05	BNG
ENSG00000101871	40.4761904761905	0.0426934459761882	-0.33158031456629	8.68758160318984E-05	BNG
ENSG00000169905	25.7142857142857	0.0267363003963852	-0.331359426161868	5.53490215236054E-14	BNG
ENSG00000187098	19.5980861244019	8.05235237869731E-10	-0.330412292260139	0.00634727754168873	BNG
ENSG00000108840	13.2352941176471	0.000480223775456203	-0.330166204586187	8.37847751568423E-06	BNG
ENSG00000205336	45.4459203036053	0.00752186156988445	-0.326567818510395	0.00273947706529407	BNG

(*continued on next page*)

Table 6 (*continued*)

id	meth.diff	meth.q	gene_fc	gene_p	
ENSG00000124788	25.7575757575758	0.0428322856458021	-0.3247633955855	5.48725590404673E-18	BNG
ENSG00000138468	19.6808510638298	0.0363634312739796	-0.324452496302909	0.000842061722170376	BNG
ENSG00000119661	10.5009584002487	0.0198710131539813	-0.324146817715437	0.00244892770308636	BNG
ENSG00000158828	22.5434024038254	9.48818804503089E-07	-0.32169317290553	0.000252368264090229	BNG
ENSG00000133059	30.0466355762825	0.0489887123582783	-0.320621897386737	0.00023545527539353	BNG
ENSG00000130723	11.3976750473101	0.000134696004589683	-0.320040985343096	0.000129242633673824	BNG
ENSG00000196352	10.062893081761	0.00946448639676561	-0.319753723653023	0.00103987762735318	BNG
ENSG00000082641	18.8746438746439	0.0413984951095962	-0.319310869004695	3.66328560649142E-11	BNG
ENSG00000213995	14.047976011994	0.0421140380563497	-0.318859345969839	0.00917522191680684	BNG
ENSG00000141736	11.1019736842105	0.015707575378512	-0.318638706904216	1.01759720474176E-05	BNG
ENSG00000196628	18.9379132532125	0.026628993901866	-0.313420129875148	3.28353137619013E-05	BNG
ENSG00000131149	41.1764705882353	0.0493532022723004	-0.312479031368485	8.88086989224702E-05	BNG
ENSG00000178234	11.5294961448808	0.00659775491842036	-0.31233732557587	0.0444075334779666	BNG
ENSG00000168056	19.5390805999268	0.00454352205309947	-0.310082881286277	0.000214762739461813	BNG
ENSG00000033122	29.625590694293	0.00210695325158986	-0.306925931548116	0.00649183678214571	BNG
ENSG00000112304	20.0174825174825	0.0351743704365662	-0.306243573211412	0.0463949995660573	BNG
ENSG00000008083	10.0729517396184	0.0140092913501159	-0.305704155228222	0.00520773838098378	BNG
ENSG00000152104	17.8128950695322	0.0289165706469852	-0.304201627678951	9.3801020593915E-09	BNG
ENSG00000156976	62.4045331362405	1.64036524813892E-26	-0.303223827036908	0.000173375292214423	BNG
ENSG00000148498	18.2381959126145	0.039148232419445	-0.302775645054516	0.000599403897821241	BNG
ENSG00000167972	29.97150997151	0.046054661618327	-0.302562770020427	0.0175183932548747	BNG
ENSG00000109654	22.3880597014925	0.0312572030696368	-0.301685799799022	0.0170642350636622	BNG
ENSG00000107104	10.1918216694849	4.13774880745456E-05	-0.300742764996734	0.00633350140038271	BNG
ENSG00000130844	27.687969924812	0.00390442314567267	-0.300668723482284	0.00719998180056289	BNG
ENSG00000185585	11.5521003818876	0.0392453693308722	-0.299045268650416	7.43191486234675E-05	BNG
ENSG00000217128	12.0838262633091	0.0017609206903326	-0.298728320110066	9.04052804294962E-05	BNG
ENSG00000099260	10.8910891089109	0.0353811040563858	-0.298592047217847	0.000424285345172563	BNG
ENSG00000091157	13.1028368794326	0.0484770918475124	-0.297059220774465	0.0374840228006454	BNG
ENSG00000140416	17.6034134584066	0.000754540256215715	-0.296072693115342	7.8888780545974E-08	BNG
ENSG00000088280	13.6121812511466	0.0043559525569461	-0.295958148559171	3.52360850016329E-05	BNG
ENSG00000196267	18.834768250973	0.0114164686143015	-0.295920444805625	0.0101731668155433	BNG
ENSG00000204217	24.3243243243243	0.00155707895508587	-0.294392145198983	8.00814045879748E-08	BNG
ENSG00000118816	17.7777777777778	0.0459158478090898	-0.293827410959701	0.000793611995264555	BNG
ENSG00000146648	21.6057812677819	0.0164588521031709	-0.293703786413115	2.29989877751664E-08	BNG
ENSG00000075568	14.4736842105263	0.028405831268229	-0.293035982058586	0.0302709234446858	BNG
ENSG00000105426	23.3977172958736	0.00158843839337624	-0.29136312889229	9.61011029442332E-06	BNG
ENSG00000142784	12.641432367221	2.75713514771609E-08	-0.291309926911496	0.000705471601159669	BNG
ENSG00000115468	24.9363327674024	0.012367393390153	-0.290583721544564	0.0401381507632302	BNG
ENSG00000119912	14.340675671213	0.0223871948498093	-0.288796061228694	0.0179505502465591	BNG
ENSG00000214655	13.1659836065574	0.0357874542093045	-0.288774708212451	0.00266065262221928	BNG
ENSG00000162825	14.2034333025851	0.00666121923321421	-0.286100015751736	0.0198036139611593	BNG
ENSG00000133424	39.5833333333333	0.0244052415164296	-0.285218427692496	0.0188359404674102	BNG
ENSG00000184677	27.8225806451613	0.0381796105921428	-0.285200061636264	0.0330078205932338	BNG
ENSG00000116005	31.1556603773585	2.10459449932301E-07	-0.28407646921438	0.000921125149288969	BNG
ENSG00000165240	10.3479853479854	0.011765225239976	-0.28314719196807	7.80285429525471E-09	BNG
ENSG00000133983	39.5604395604396	0.0414994516121064	-0.28200331050987	0.0264347269628561	BNG
ENSG00000151553	18.560074801309	0.0421356350946662	-0.280613980013202	0.00535868165740882	BNG
ENSG00000186448	20.9177489177489	0.000190407930326322	-0.279901421655579	0.0243344047039009	BNG
ENSG00000139266	11.5023275497249	0.0251514349771169	-0.277918279325949	0.0404238161915395	BNG
ENSG00000164855	17.4666035744185	0.00378786634448218	-0.268774379016911	0.0101022767524733	BNG
ENSG00000054965	28.4817875726967	0.0118905351512364	-0.267963637356679	0.000293100155619997	BNG
ENSG00000148842	28.0701754385965	0.0148914319157164	-0.267695783203657	0.00377595052802898	BNG
ENSG00000123636	12.257053291536	0.0303309564762876	-0.267416852462943	0.011351823485927	BNG
ENSG00000115170	12.5139206377117	0.0109195293972354	-0.267382852871544	0.0370125180568233	BNG
ENSG00000133639	18.9965359258018	0.0137735837044225	-0.267168024889054	0.00289962439444354	BNG
ENSG00000126858	19.9737532808399	0.0103436202041154	-0.266499681624815	0.0311298311886331	BNG
ENSG00000112855	11.1111111111111	0.0274407754224659	-0.264771736543482	0.0349592186244644	BNG
ENSG00000162434	11.1013986013986	0.0400147705940586	-0.263612329451374	4.94379178207903E-08	BNG
ENSG00000140379	-13.0602240896359	0.0419869667954231	7.75933340719466	0.0367406623189661	BNG
ENSG00000102445	-22.4608590927338	0.0136717844177114	7.1632303488683	0.0201523496528516	BNG
ENSG00000198626	-30.4647160068847	0.0317766894353491	5.4374053123073	0.0297721172788166	BNG
ENSG00000273217	-11.6228070175439	0.0495363996427847	5.32192809488736	0.0445013525732622	BNG
ENSG00000186603	-10.4218502246818	1.74723393165367E-06	4.88264304936184	0.00562268869170042	BNG
ENSG00000167772	-20.6896551724138	0.026213853591628	2.89710009241571	3.24861125698761E-10	BNG
ENSG00000288520	-18.5674522845575	0.0293128390705597	2.7004397181411	0.0288626152504842	BNG
ENSG00000152953	-25.4347826086957	0.0389556921466233	2.32192809488736	0.0352806015308715	BNG
ENSG00000163359	-18.6857721812129	0.00839883744965913	2	0.0453917622597636	BNG
ENSG00000197641	-11.5761478163494	0.00503948227834267	1.92619869958988	1.92719648884193E-25	BNG
ENSG00000205403	-15.8402203856749	0.0062625386976592	1.68182403997374	0.0124171144084143	BNG
ENSG00000138675	-13.9705882352941	0.00218543164097531	1.58496250072116	0.00663087291080351	BNG
ENSG00000178726	-11.8489223129544	0.00199516551116929	1.52281005197375	2.48269726859935E-30	BNG
ENSG00000154678	-19.3846556690233	0.0433527558360389	1.39854937649027	0.0282987501155144	BNG
ENSG00000130164	-11.0260942983035	0.0115934255677052	1.38476472870143	1.68437434910057E-68	BNG
ENSG00000138944	-37.8117457763475	0.0169445660029793	1.37586690199816	0.00219311995651581	BNG
ENSG00000197646	-12.0122574055158	0.0251916789947428	1.36950657725287	4.76360889303288E-20	BNG

Table 6 (*continued*)

id	meth.diff	meth.q	gene_fc	gene_p	
ENSG00000163485	-17.520151730678	0.00250341105617622	1.34513548604869	0.0424124417976442	BNG
ENSG00000188001	-21.5264586160109	0.00189270004090834	1.33763299559323	1.51293275212706E-05	BNG
ENSG00000285816	-15.6369183829138	0.0239049278657468	1.29972421516298	1.68350938440851E-07	BNG
ENSG00000177374	-21.5589376667475	0.00445208163839317	1.24285652389617	0.0138731645825835	BNG
ENSG00000090339	-10.6666666666667	0.0410133958281216	1.22517486200778	1.17341214937116E-27	BNG
ENSG00000104368	-34.1463414634146	0.0182409938245087	1.1794767156618	4.32168441024132E-39	BNG
ENSG00000169991	-17.1866447728517	0.0158204811842248	1.15497288407955	1.9806121954697E-32	BNG
ENSG00000175505	-27.9661016949153	1.06348633808996E-05	1.13024667675028	7.38979815808529E-11	BNG
ENSG00000196639	-15.4970760233918	0.00090947165898245	1.12687176584051	2.79229839886979E-11	BNG
ENSG00000196083	-36.3636363636364	0.000249970412403766	1.1188160178939	1.91714465012516E-34	BNG
ENSG00000107957	-18.655090765588	0.043587140391366	1.10378045790299	5.22642208471637E-05	BNG
ENSG00000167914	-19.7192513368984	0.00810848185643203	1.0790715709912	0.00212095639712	BNG
ENSG00000124496	-11.9527769853635	0.00548776059044123	1.05475976867859	9.74227997345186E-09	BNG
ENSG00000134107	-20.5533596837945	0.0102286108939419	1.01740704590947	5.59821544185794E-34	BNG
ENSG00000112096	-15.7002858309514	0.0276978683819853	1.00829655641631	0.0277179645543597	BNG
ENSG00000136026	-20.8110516934046	5.06625982084557E-06	0.981140972748685	0.000121641120032545	BNG
ENSG00000137936	-11.6054875787913	0.0387043048384392	0.940973373349762	1.93812440346207E-27	BNG
ENSG00000125730	-12.3979591836735	0.000755350080859917	0.940197017497937	1.10578488599274E-13	BNG
ENSG00000142634	-25.2007557864903	0.0255231120152627	0.908622445824029	4.92613125327356E-49	BNG
ENSG00000182326	-12.3648537401899	0.0273998846984687	0.878141657126903	3.79553006148258E-05	BNG
ENSG00000111700	-51.4193548387097	0.00599089375902751	0.867939147909315	0.0025682878525908	BNG
ENSG00000129521	-35.8974358974359	0.00643442018997199	0.84358980503217	2.59806804251617E-05	BNG
ENSG00000075131	-13.2420091324201	0.0289563274100958	0.816530118457942	0.00474497942871165	BNG
ENSG00000114541	-14.0845070422535	0.034354834947395	0.815747086313056	1.42922170794235E-22	BNG
ENSG00000127507	-23.5303617571059	0.00980477148159086	0.810338780496422	0.000547643416920011	BNG
ENSG00000172927	-16.2748744136993	0.0160248077870733	0.808903709153095	0.00348914353770542	BNG
ENSG00000174640	-20.5257054503286	0.029565719454343	0.800012946716431	0.00209466071836222	BNG
ENSG00000156299	-17.5735294117647	0.0277298044419221	0.792603966282472	5.65041318074885E-06	BNG
ENSG00000088727	-18.2795698924731	0.0496766885347703	0.787318886643381	0.0218939732192762	BNG
ENSG00000105137	-11.5606936416185	0.00939974597671166	0.786429083203057	0.000279118337134963	BNG
ENSG00000128965	-18.6904761904762	0.000282827758537118	0.782165860625856	1.505866464105E-06	BNG
ENSG00000103546	-11.6170689719897	0.0154089401089322	0.758806642705791	0.0418443211370969	BNG
ENSG00000123358	-25.8726647000983	0.0130489763385992	0.737561626003184	5.9249188956385E-06	BNG
ENSG00000138829	-31.6725352112676	0.0372853032268371	0.713477241243836	0.0417689085213096	BNG
ENSG00000102743	-18.4110885733604	0.00457691456434629	0.707392478782857	0.00209427175210604	BNG
ENSG00000157557	-22.9957805907173	0.017203962372102	0.694034680852988	1.74996558874179E-33	BNG
ENSG00000034152	-18.8859520313265	0.0167888007588856	0.693086631049928	5.24816371136761E-05	BNG
ENSG00000213397	-27.1225071225071	0.00434588003696628	0.689932060322699	0.000404367736333311	BNG
ENSG00000131746	-10.5288590604027	0.0264465832690492	0.678937554055473	5.60206611487306E-12	BNG
ENSG00000165799	-24.1837299391256	0.00857990103345192	0.678071905112639	0.0177003751106127	BNG
ENSG00000142089	-11.331290432414	5.65365659019406E-05	0.673593087060183	1.29781289919547E-25	BNG
ENSG00000184408	-38.2692307692308	9.49729224589839E-06	0.667424660913128	0.0384781428522723	BNG
ENSG00000126091	-21.6867469879518	0.00889633435336452	0.626850897011178	0.00839083915114877	BNG
ENSG00000143322	-26.9976498237368	0.000254774068165335	0.617742991222575	1.13702174725912E-26	BNG
ENSG00000127666	-13.0050658561297	0.00325853898090201	0.617666665793861	2.82406615980706E-06	BNG
ENSG00000154217	-23.3516483516484	0.0493895123654999	0.615899482470343	0.000662697989781469	BNG
ENSG00000112159	-23.3950694531348	0.0108221249561433	0.610708775591004	0.00592967658047154	BNG
ENSG00000104419	-23.7073170731707	0.049221174709303	0.609880299095611	1.42913107270399E-30	BNG
ENSG00000182010	-17.0862470862471	0.0355002358593476	0.597418933145846	1.36143320589088E-07	BNG
ENSG00000107937	-16.5659543109801	2.71661545092223E-06	0.597234370126258	1.09995147692887E-07	BNG
ENSG00000119681	-19.1963826944815	0.00719070703708989	0.595560346860678	1.84681312504672E-05	BNG
ENSG00000128294	-29.5713229859571	0.000142543647709696	0.59321592735501	0.0345827448979271	BNG
ENSG00000154655	-33.4452064789143	0.00390173354630116	0.59183345241	1.03930323127386E-06	BNG
ENSG00000165650	-16.3934426229508	0.0378421421189818	0.579453598291972	0.0453755163033109	BNG
ENSG00000140945	-54.1404612159329	6.28268106238419E-05	0.574978412148533	0.00366332390862918	BNG
ENSG00000131941	-10.5882516781327	0.0184141127143809	0.573258396588686	1.74407845148977E-14	BNG
ENSG00000136492	-11.7223083063342	0.0117767722940519	0.572251448971601	2.26692368906575E-07	BNG
ENSG00000166444	-42.5475687103594	0.0295866997565394	0.56545984417481	4.99627819602438E-09	BNG
ENSG00000156113	-17.9012547914687	0.0127279978159161	0.562791119722535	0.0227562050853387	BNG
ENSG00000159110	-14.3515151515151	0.00553207872317444	0.562541206013363	0.0121492862435441	BNG
ENSG00000113318	-17.8626289225368	0.00157714237650006	0.562313761775957	0.000273593476721578	BNG
ENSG00000142185	-42.8235294117647	0.0245087649772323	0.561438218660123	0.0293332076847108	BNG
ENSG00000050820	-20.3125	0.0271861387486728	0.556139137843372	4.24342943708694E-08	BNG
ENSG00000115641	-24.035964035964	0.0339725594017967	0.552391837873705	1.0526762753976E-29	BNG
ENSG00000060558	-13.6	0.00601386696065428	0.550616755318472	0.00025669154956774	BNG
ENSG00000147065	-19.4475138121547	0.0241049580541904	0.53654301642417	8.11287354734939E-30	BNG
ENSG00000160214	-12.9454545454545	0.0390164434434383	0.535814851392069	1.07390707704074E-05	BNG
ENSG00000162419	-12.7713474557764	0.0319921945269321	0.525155335489124	0.00223599875365847	BNG
ENSG00000167670	-11.6883116883117	0.0192095726179785	0.521039303621415	0.000147383634918683	BNG
ENSG00000171488	-12.2956730769231	0.0172368472444858	0.513239813177653	0.00114332064975316	BNG
ENSG00000073712	-16.9811320754717	0.0408786639650407	0.512037234330269	1.28218578484813E-07	BNG
ENSG00000196792	-31.4427103159497	0.000199788774540287	0.507954281998884	0.0461085059867358	BNG
ENSG00000050165	-16	0.049872192771084	0.507308499457133	1.72938165941866E-06	BNG
ENSG00000171453	-13.2422402159244	0.0269713990389909	0.50397390606564	1.80289167441687E-05	BNG

(*continued on next page*)

Table 6 (*continued*)

id	meth.diff	meth.q	gene_fc	gene_p	
ENSG00000147689	-10.2777205394143	0.0296131818152576	0.498448488864361	2.63996760589321E-05	BNG
ENSG00000134686	-11.2458193979933	0.0490807313383056	0.49406131874452	5.10831089048732E-11	BNG
ENSG00000065534	-26.1363636363636	4.58581903515231E-05	0.492937258882307	0.00489440648365668	BNG
ENSG00000123130	-31.9319319319319	0.0018567584274336	0.489750774803252	0.00176615938851862	BNG
ENSG00000275740	-15.503581963759	0.0453593619314214	0.487931412162827	0.00587654338965406	BNG
ENSG00000156398	-18.8524590163934	0.000348784129373148	0.487008729785849	0.0128476275418884	BNG
ENSG00000285901	-12.202502379981	0.00468928631103516	0.485665901665924	0.00265331917593365	BNG
ENSG00000039560	-12.9437229437229	0.0263720785924747	0.483171930628531	6.66514055683011E-11	BNG
ENSG00000100023	-22.8361871673974	0.00133219128075895	0.482668327207678	0.0105207229595894	BNG
ENSG00000182484	-20.2096926023306	0.0481433701401008	0.48255939531705	0.0492338919447914	BNG
ENSG00000132334	-10.0267752552016	0.0242987932391369	0.475178385333266	7.6377217442228E-05	BNG
ENSG00000083454	-14.9709934735315	0.0364912699901172	0.474966356535059	0.036003407428261	BNG
ENSG00000076003	-11.8291944276196	0.0218100885442315	0.473426901781583	1.34801366061123E-12	BNG
ENSG00000177706	-13.3480709381021	2.24772238051684E-13	0.471523213919535	5.28191185180264E-07	BNG
ENSG00000100065	-20.1939115929942	0.0130722284127865	0.470268230654617	3.15996374866782E-08	BNG
ENSG00000173530	-21.7687985014718	2.8140664777479E-05	0.468398314663583	0.000143462486375593	BNG
ENSG00000137478	-24.3654822335025	1.64835961175456E-10	0.46837326134002	0.00725447648208387	BNG
ENSG00000171132	-21.3210296260321	0.0256886794368254	0.468248157279246	0.0072417886941382	BNG
ENSG00000149177	-10.7919678714859	0.00278325904974516	0.467617414400212	0.0446129236346782	BNG
ENSG00000185215	-22.6086956521739	0.0223192198423381	0.466484134892728	5.69006853725303E-12	BNG
ENSG00000103187	-11.2068965517241	0.0387775128062209	0.46390663278	2.51230178927757E-17	BNG
ENSG00000134013	-18.2029598308668	0.0190547132705856	0.462967204381542	4.76544917479903E-12	BNG
ENSG00000141682	-10.1941747572816	0.00214392520301642	0.462655005004157	1.81835401657973E-05	BNG
ENSG00000134775	-15.8536585365854	0.0272829985423177	0.459090918425327	3.0528769923768E-05	BNG
ENSG00000188677	-24.9844564541585	0.000168636053320139	0.45812961249548	0.0430808758707585	BNG
ENSG00000240053	-12.7484296158995	0.0296606338382643	0.455843715666729	0.0294401639525279	BNG
ENSG00000160799	-40.3155818540434	1.69713921674551E-06	0.452833529552961	0.00501376556672779	BNG
ENSG00000109861	-12.7042483660131	0.0431789067221677	0.448219439704906	4.16593315448456E-10	BNG
ENSG00000157551	-12.9955514265807	0.00753561613606589	0.447594054452798	0.00230304213579688	BNG
ENSG00000197498	-13.6572622779519	0.0123223125411247	0.447023051589182	0.00184985462302071	BNG
ENSG00000196776	-11.6533425279246	0.00849214239415063	0.437581426271295	0.000188816039026614	BNG
ENSG00000197417	-19.751056964842	4.01914267959484E-11	0.432638130125041	0.0169974449289784	BNG
ENSG00000092969	-12.7301640441915	0.0319446080797506	0.432025567700634	1.3965214654066E-08	BNG
ENSG00000148459	-31.8840579710145	0.00568478148180565	0.429364974832301	0.0433078449692255	BNG
ENSG00000162433	-11.2694811599921	0.00173237839008872	0.425793896102561	4.5580052209163E-08	BNG
ENSG00000101546	-10.7843137254902	0.0418187681953032	0.423722096644087	0.00495092158758691	BNG
ENSG00000120254	-11.3635157369566	0.0402595578220733	0.416225112127262	3.11356337626985E-05	BNG
ENSG00000165689	-12.2080440996325	1.88001695122534E-05	0.414491747412722	2.01925319811362E-07	BNG
ENSG00000166949	-12.8427912028238	0.0166308090053364	0.410357367727777	6.43088240364512E-15	BNG
ENSG00000139343	-16.9364413656437	0.00648669118839666	0.408633088879767	0.000641235169794379	BNG
ENSG00000166068	-13.5135135135135	0.0351743704365662	0.40489548885823	0.000120660653415139	BNG
ENSG00000105928	-11.1111111111111	0.035093062877173	0.40377048746052	4.22656711665809E-06	BNG
ENSG00000141076	-14.051533802869	0.0280107819608233	0.401002142074746	4.02203339977718E-15	BNG
ENSG00000156787	-29.8706240487062	0.0468147702659847	0.395736943319907	4.74318720256828E-05	BNG
ENSG00000170379	-32.4734249416645	0.0170665902919789	0.394768901772857	0.0271338669211037	BNG
ENSG00000146232	-14.0488110137672	0.00474973349274566	0.392149770861626	0.00332674089463065	BNG
ENSG00000079337	-14.4724556489262	0.0405054892640396	0.390891411947141	0.0064912127527941	BNG
ENSG00000113356	-10.45280468574	0.0174053941207476	0.390375445044573	0.0389512379357209	BNG
ENSG00000126602	-10.4268292682927	0.00276913810072556	0.38577551135716	1.82359994148375E-09	BNG
ENSG00000132470	-11.2192569335427	0.00310423617780924	0.383379173420695	4.30403166435463E-06	BNG
ENSG00000012048	-16.2792058516196	2.78883070497941E-05	0.381249185822562	2.9090055172466E-05	BNG
ENSG00000173744	-14.4028520499109	0.000202174864163991	0.379563150298012	0.00111750633730919	BNG
ENSG00000276043	-20.8995584988963	0.0126091804239962	0.377966627324228	1.13351188388114E-08	BNG
ENSG00000104998	-31.9047619047619	0.00809423555363895	0.377373601776779	0.00378313393633686	BNG
ENSG00000020426	-13.6842105263158	0.0110742001662289	0.372042127924171	0.0012578498521631	BNG
ENSG00000109519	-11.2951807228916	0.0396862905145413	0.37164683450387	0.000248352981138557	BNG
ENSG00000117411	-17.4176805078022	0.0164899944153455	0.370426330875051	5.04544077240487E-06	BNG
ENSG00000072110	-21.177245601798	0.00391150829143861	0.36814862841075	2.13959571937118E-10	BNG
ENSG00000143324	-18.1824882075472	9.45950789324614E-06	0.366843989575849	3.25957742537955E-05	BNG
ENSG00000174501	-20.0966962127317	0.0310230617351151	0.36513259345253	0.00490678291116583	BNG
ENSG00000132434	-27.9419609516697	0.0393749617732968	0.363383323510468	0.0187163147277958	BNG
ENSG00000185344	-27.9569892473118	3.86317235533345E-06	0.361820822010875	0.0321913603940228	BNG
ENSG00000198742	-16.2399969659043	0.00501008174211403	0.360277274531718	0.000538983577484304	BNG
ENSG00000151693	-25.9456333140544	2.19912826474313E-05	0.354638036216122	4.57279940276897E-06	BNG
ENSG00000156795	-38.0377358490566	0.0144869300714228	0.343348146097523	0.00551779589047665	BNG
ENSG00000077150	-12.6892461370376	0.0306893423114589	0.341242850796 5	3.37086858397517E-05	BNG
ENSG00000108021	-22.2047389855609	0.00106602646373337	0.339704174053552	0.000135551547207724	BNG
ENSG00000119408	-61.0294117647059	2.8440811599222E-06	0.338972363751516	0.00265932587383534	BNG
ENSG00000197063	-15.2279763580073	0.00842915807812787	0.334400889337693	5.31922911707779E-05	BNG
ENSG00000180730	-20.8983251564879	7.90954011912372E-07	0.333836788722445	0.00201645424663414	BNG
ENSG00000111252	-11.7093023255814	0.00998741143562405	0.33125115813949	3.52825565234949E-05	BNG
ENSG00000145819	-10.7178340784898	0.0396605018365575	0.330677158225405	0.00536155887245511	BNG
ENSG00000196535	-11.4600972797694	0.0161093684855209	0.328931310926499	0.0123758316344305	BNG
ENSG00000162613	-17.3644474948524	0.0324067530449809	0.328447709136984	3.13022134509149E-06	BNG
ENSG00000062038	-13.4920634920635	0.0238922126161395	0.328215850647634	2.00014818397733E-10	BNG
ENSG00000092853	-15.9663865546218	0.0125512798926505	0.327634213232578	0.000642703698649307	BNG

Table 6 (*continued*)

id	meth.diff	meth.q	gene_fc	gene_p	
ENSG00000092470	-29.1854072963518	0.0296202538605799	0.326458938833974	0.0020964526533321	BNG
ENSG00000186314	-17.1071438989528	0.0231358749611893	0.326345262946965	0.0329328808988499	BNG
ENSG00000166166	-10.68524970964	0.0192164922708738	0.325728283849324	0.0136212340309268	BNG
ENSG00000196550	-12.6049933383537	0.013463315146511	0.323951510423659	0.00514137736104517	BNG
ENSG00000104852	-10.1283636828863	0.0139631200255514	0.320980373575367	0.0272299406051771	BNG
ENSG00000165304	-18.1269162872805	0.000643598541175108	0.319129648728101	2.3370565052397E-05	BNG
ENSG00000214113	-12.5010029687876	0.0156887342030493	0.31875051786639	0.0469611212957108	BNG
ENSG00000138442	-13.8278388278388	0.0213187887833145	0.318574659777552	4.27600892666218E-05	BNG
ENSG00000112972	-16.1152949614488	0.0126838220569589	0.315001497982013	0.000188738979456314	BNG
ENSG00000169180	-13.2955936352509	0.000849752872498409	0.314632885879975	0.00135627094179664	BNG
ENSG00000049541	-12.280701754386	0.0169546622797692	0.31359405800916	0.0156478701318847	BNG
ENSG00000132676	-11.035419452049	0.0245033065121283	0.312063598061888	0.000208407937187256	BNG
ENSG00000141526	-23.1404958677686	0.00261240939848165	0.311619739598562	0.000591786040639583	BNG
ENSG00000126698	-25.1425106124924	0.00166587580328008	0.306617549211211	5.18237372697286E-05	BNG
ENSG00000114480	-10.9884201819686	0.0223217340619718	0.306344199668908	0.00604581620290016	BNG
ENSG00000120539	-19.3901132968829	0.00343396625615726	0.305597893946784	0.00455858021237978	BNG
ENSG00000105486	-15.5844155844156	0.0453494958684685	0.30478296776648	0.0373791119128896	BNG
ENSG00000131620	-13.3653830413027	0.0252948591576672	0.303751434937819	0.00347391075687533	BNG
ENSG00000254087	-10.2983725135624	0.0488287796275528	0.300166838538387	3.02913127470451E-07	BNG
ENSG00000035403	-11.7315415508187	0.0441497518533752	0.299008368980096	6.87026731676217E-09	BNG
ENSG00000083635	-19.9529373580006	0.0381200922165914	0.29870686861847	0.0119954298989839	BNG
ENSG00000004897	-11.1111111111111	0.00478915076025825	0.295393259079194	0.0046684259107152 4	BNG
ENSG00000050344	-10.0816582914573	0.015707575378512	0.293012352905917	1.17008748072877E-05	BNG
ENSG00000153179	-21.377606263361	0.0203578875585219	0.292518165356911	7.62622000548776E-07	BNG
ENSG00000160957	-23.3835005574136	0.00101322585276091	0.290326906767959	0.0265100950636294	BNG
ENSG00000163808	-18.9340915718868	0.00301633219510026	0.289017609465231	0.0494132444071175	BNG
ENSG00000178409	-12.9095116307393	0.000364087446723097	0.2883218952718	0.00811924789522798	BNG
ENSG00000175054	-11.7296606644084	0.00106320574342346	0.287648371836303	0.0146795244446537	BNG
ENSG00000173039	-27.7398958591619	0.00656136475063831	0.285633241047627	0.0231883773624121	BNG
ENSG00000150753	-14.4251968503937	0.0218407491899384	0.284904189377523	1.84163220481641E-11	BNG
ENSG00000107130	-14.7435897435897	0.00549774755816806	0.281455174998768	0.000936775496395401	BNG
ENSG00000100749	-18.5744810744811	0.0250788833752389	0.280627114774547	0.00344286194449417	BNG
ENSG00000183856	-13.0434782608696	0.0401499412717785	0.279732061639544	5.33521552830561E-05	BNG
ENSG00000175792	-10.6004901960784	0.00203845771080645	0.279137832001109	0.000439440796344355	BNG
ENSG00000074201	-24.7899159663866	0.0403083767489215	0.278172389751471	0.00542221796366029	BNG
ENSG00000184900	-30.8723265153638	0.000377128553514499	0.273174201869466	0.000220867190177533	BNG
ENSG00000105220	-18.7007110536522	0.00212214059295916	0.272702090740145	0.00812206968916581	BNG
ENSG00000163293	-10.8718487394958	0.0497617848609876	0.272023189061049	0.0270981163833197	BNG
ENSG00000131378	-41.025641025641	0.00822190406098067	0.271778685197926	0.0160680013219797	BNG
ENSG00000001497	-16.4869398514258	0.0137608208710987	0.268705941554237	0.00102904917257424	BNG
ENSG00000135932	-13.8342133248755	0.000662445859206366	0.267400192087818	4.11766224712256E-06	BNG
ENSG00000285077	-15.7713467817686	0.045902210404969	0.266423004081944	0.0468961829118312	BNG
ENSG00000156873	-12.9756450446106	0.000127244227100649	0.265336666731864	0.031407509745278	BNG
ENSG00000182022	-14.7592262313075	0.00110428414136549	0.26444863953694	0.000757398141982721	BNG

3.10. Establishment and identification of the TEC ageing model and a coculture model of MSCs

Fourth-generation TECs were collected, the cell concentration was adjusted to 5×10^5 L-1, and 100 μL of cell suspension was inoculated in a 6-well culture plate. When the cell density was approximately 80%, 200 μmol/L H_2O_2 (China Nanguo Pharmaceutical Co., Ltd.) was added, and the cells were cocultured for 72 h. Fourth-generation MSCs were collected, the cell concentration was adjusted to 5×10^5 L-1, 100 μL of cell suspension was inoculated into the Transwell chamber, the Transwell chamber was embedded in the upper layer of the 6-well culture plate, and DMEM/F12 containing 10% fetal bovine serum was used for coculture of cells for 48 h.

3.11. SA-β-gal (senescence-associated β-galactosidase) staining

TECs were collected, washed with PBS once, operated according to the kit instructions (Solarbio, G1580), and observed under an ordinary optical microscope (ZEN2011), and the number of blue-positive cells in three visual fields was counted.

3.12. Expression level analysis of P21 and P16

TECs was collected for Western blotting analysis and lysed in RIPA buffer (Solarbio, China, Beijing). The total proteins of TEC cells were separated by Tris-Gly and 10% gel electrophoresis and then transferred to a nitrocellulose membrane. The cell membrane was blocked with 5% skim milk at room temperature for 1.5 h and then incubated with an antibody overnight. The next day, the membrane was washed with PBST and incubated for 30 min with horseradish peroxidase-labeled secondary antibody. Protein bands were detected after treatment with SuperSignal West Femto (Thermo Fisher Science, Waltham, MA, USA). Primary anti-rabbit anti-human P16 (1RV 1000, ab32503), P21 (1RV 1000, ab32351), SRC (1RV 300000 ab179473 ab109381), and ITGB3 (1RV 1000 ab179473) antibodies were obtained from Abcam. The primary anti-rabbit anti-human β-actin antibody (1RV 25000~66009-1-Ig) and the secondary anti-HRP-Goat IgG antibody (1RV 1000, SA00001-2) were purchased from Proteintech.

3.13. Cell apoptosis assay

TUNEL staining was used to determine the apoptosis of TECs. TECs were collected, paraformaldehyde was fixed, the fixating solution was removed, 100 μl film breaking working solution was added, incubated at room temperature for 20 min, washed 3 times with PBS for 5 min each time, and buffer was added to cover the tissue for 10 min. Appropriate amounts of TDT enzyme and dUTP in the TUNEL kit were mixed with buffer at a 1:5:50 ratio. The slides were

Table 7
Transcription factors correlate with target genes.

TF	Gene	Score
ELL2	TRIM7	4.465
ELL2	TRIM41	4.317
ELL2	HMGN4	3.913
ELL2	BORCS6	3.857
ELL2	ALOXE3	3.803
ELL2	ZNF184	3.755
ELL2	RNF207	3.587
ELL2	HES7	3.579
ELL2	H4C12	3.578
ELL2	AURKB	3.566
ELL2	UBC	3.538
ELL2	H4C8	3.514
ELL2	SDR39U1	3.409
ELL2	B4GALT3	3.336
ELL2	GBA	3.3
ELL2	SHF	3.265
ELL2	HARS2	3.246
ELL2	HARS1	3.242
ELL2	PPOX	3.235
ELL2	USP21	3.14
ELL2	PQBP1	3.138
ELL2	H4C11	3.132
ELL2	ZMAT2	3.117
ELL2	H2AC11	3.113
ELL2	SRCIN1	3.098
ELL2	H2BC11	3.097
ELL2	TIMM17B	3.093
ELL2	ANG	3.084
ELL2	RPL22	3.082
ELL2	H2BC17	3.079
ELL2	CCDC77	3.075
ELL2	H2AC17	3.063
ELL2	H4C9	3.009
ELL2	RNASE4	3.003
ELL2	ZNF335	3.002
ELL2	HOXA5	2.98
ELL2	WDR13	2.958
ELL2	S100A13	2.946
ELL2	BDP1	2.942
ELL2	S100A1	2.935
ELL2	PIN1	2.91
ELL2	H2AC15	2.884
ELL2	HBP1	2.875
ELL2	LDHA	2.875
ELL2	LOC105371063	2.872
ELL2	BAZ2A	2.865
ELL2	CALM1	2.861
ELL2	DNAJA3	2.858
ELL2	LOC107985657	2.853
ELL2	BRMS1	2.844
ELL2	CCDC130	2.842
ELL2	H2BC15	2.837
ELL2	TMEM107	2.836
ELL2	KHK	2.821
ELL2	ZBED9	2.818
ELL2	UFC1	2.793
ELL2	CSKMT	2.774
ELL2	UBL5	2.772
ELL2	C11orf98	2.767
ELL2	H2BC9	2.748
ELL2	TMEM205	2.738
ELL2	TCEANC	2.733
ELL2	RACK1	2.733
ELL2	H3C7	2.733
ELL2	DPP9	2.732
ELL2	B4GAT1	2.717
ELL2	FAM189B	2.714
ELL2	RIN1	2.708
ELL2	CCDC159	2.707
ELL2	LBHD1	2.703
ELL2	UQCC3	2.7
ELL2	SLC25A35	2.699
ELL2	GCDH	2.685
ELL2	ZNF775	2.685

Table 7 (*continued*)

TF	Gene	Score
ELL2	DISP3	2.682
ELL2	ALG3	2.679
ELL2	CORO7	2.675
ELL2	CORO7-PAM16	2.675
ELL2	WBP1	2.674
ELL2	NOD1	2.671
ELL2	MUC1	2.663
ELL2	NCOA3	2.661
ELL2	EEF1AKMT4	2.657
ELL2	EEF1AKMT4-ECE2	2.657
ELL2	H3C8	2.655
ELL2	INO80B	2.643
ELL2	QRICH1	2.639
ELL2	INTS5	2.636
ELL2	BSDC1	2.635
ELL2	TP53I3	2.633
ELL2	BSG	2.632
ELL2	IER3	2.631
ELL2	JUP	2.629
ELL2	H3C12	2.624
ELL2	H2BC10	2.624
ELL2	SIRT4	2.616
ELL2	SCAMP3	2.609
ELL2	PSAP	2.608
ELL2	HSPA6	2.607
ELL2	H4C2	2.605
F2R	MTRNR2L1	0.888
F2R	COL23A1	0.727
F2R	LOC105378947	0.482
F2R	TMEM242	0.481
F2R	ARHGEF18	0.464
F2R	LOC101060017	0.244
F2R	PEX11G	0.07
F2R	CLK4	0.057
F2R	OR4F16	0.046
F2R	TEX45	0.039
F2R	MMEL1	0.029
F2R	POTEA	0.026
F2R	FRG2B	0.013
F2R	ZNF358	0.011
F2R	ZDHHC14	0.009
F2R	MCOLN1	0.007
F2R	PNPLA6	0.003
F2R	PRXL2B	0.001
F2R	HGSNAT	0.001
F2R	LOC107984841	0.001
F2R	TTC34	0.001
GMEB2	UBE2M	3.861
GMEB2	CHMP2A	3.676
GMEB2	TAF6	3.455
GMEB2	CNPY4	3.448
GMEB2	MCM7	3.444
GMEB2	AP4M1	3.442
GMEB2	SRSF2	3.395
GMEB2	MFSD11	3.394
GMEB2	VPS52	3.39
GMEB2	RPS18	3.39
GMEB2	ZNF517	3.264
GMEB2	B3GALT4	3.233
GMEB2	RPL8	3.126
GMEB2	MOGS	3.116
GMEB2	WBP1	3.081
GMEB2	MZF1	3.074
GMEB2	NAA80	3.062
GMEB2	HYAL3	3.062
GMEB2	HYOU1	2.977
GMEB2	LIN37	2.974
GMEB2	PROSER3	2.974
GMEB2	WDR74	2.969
GMEB2	TASOR	2.929
GMEB2	HSPB6	2.92
GMEB2	TAF12	2.911
GMEB2	YIF1B	2.909
GMEB2	MRPL53	2.894
GMEB2	C19orf33	2.879

Table 7 (*continued*)

TF	Gene	Score
GMEB2	NAA38	2.872
GMEB2	USP21	2.871
GMEB2	INO80B	2.87
GMEB2	COPS6	2.866
GMEB2	CYB5D1	2.865
GMEB2	MBLAC1	2.855
GMEB2	DBP	2.842
GMEB2	PSENEN	2.84
GMEB2	TUSC2	2.835
GMEB2	U2AF1L4	2.824
GMEB2	SEC22C	2.814
GMEB2	GLTPD2	2.804
GMEB2	CKS1B	2.803
GMEB2	TRIM28	2.796
GMEB2	SHC1	2.793
GMEB2	KCNK6	2.786
GMEB2	CALR	2.786
GMEB2	DHPS	2.777
GMEB2	RAD23A	2.776
GMEB2	SS18L2	2.776
GMEB2	TMEM88	2.764
GMEB2	ZNF34	2.763
GMEB2	PCSK4	2.755
GMEB2	PPOX	2.74
GMEB2	REEP6	2.726
GMEB2	COG8	2.724
GMEB2	HYAL2	2.72
GMEB2	NIP7	2.718
GMEB2	RPL10	2.678
GMEB2	WDR46	2.674
GMEB2	PFDN6	2.673
GMEB2	UFC1	2.662
GMEB2	ZNF497	2.655
GMEB2	RASSF1	2.653
GMEB2	RPS2	2.651
GMEB2	H2BC6	2.65
GMEB2	RPL26	2.647
GMEB2	VPS11	2.646
GMEB2	ZNF837	2.645
GMEB2	RPS5	2.644
GMEB2	ZNF668	2.641
GMEB2	TP53I3	2.637
GMEB2	ZNF646	2.629
GMEB2	RXRB	2.621
GMEB2	SLC39A7	2.62
GMEB2	HYAL1	2.614
GMEB2	H4C4	2.609
GMEB2	EID2	2.605
GMEB2	YDJC	2.604
GMEB2	PSMB6	2.601
GMEB2	CDC37	2.6
GMEB2	TBCB	2.6
GMEB2	H2AX	2.592
GMEB2	NDUFB10	2.592
GMEB2	PIH1D1	2.592
GMEB2	ZBTB45	2.589
GMEB2	TRMT112	2.579
GMEB2	ZC3H4	2.577
GMEB2	FKBP2 / LOC114841035	2.575
GMEB2	LOC114841035	2.575
GMEB2	FOS	2.575
GMEB2	POLR2I	2.568
GMEB2	ALDH16A1	2.553
GMEB2	NUP155	2.552
GMEB2	IDE	2.548
GMEB2	DCTPP1	2.548
GMEB2	STX5	2.545
GMEB2	MNT	2.545
GMEB2	RSRP1	2.543
GMEB2	BICRA	2.542
GMEB2	GNL1	2.542
GMEB2	SYF2	2.54
METLL1	METTL14	4.893
METLL1	C12orf57	1.67

(*continued on next page*)

Table 7 (*continued*)

TF	Gene	Score
METLL1	PTPN6	1.387
METLL1	TEX14	1.374
METLL1	LOC730183	1.057
METLL1	FBRS	1.04
METLL1	SRCAP	1.007
METLL1	EIF2B3	1
METLL1	TRMT2A	0.999
METLL1	DNAJC11	0.999
METLL1	ARHGAP24	0.999
METLL1	CDCA5	0.998
METLL1	CLUAP1	0.998
METLL1	C7orf26	0.998
METLL1	NIPSNAP2	0.997
METLL1	ARHGEF2	0.997
METLL1	THEM6	0.997
METLL1	SLC45A4	0.997
METLL1	TAF12	0.996
METLL1	R3HCC1	0.995
METLL1	BAIAP2	0.995
METLL1	DRAP1	0.995
METLL1	POLR2I	0.995
METLL1	ABHD16A	0.995
METLL1	RAB37	0.995
METLL1	DHX16	0.994
METLL1	FOXP4	0.993
METLL1	AURKAIP1	0.993
METLL1	KRBA2	0.993
METLL1	SUPT4H1	0.993
METLL1	PPIL2	0.992
METLL1	KCTD5	0.992
METLL1	ZFPL1	0.992
METLL1	TMEM14B	0.99
METLL1	DPP9	0.99
METLL1	RANBP1	0.99
METLL1	TMEM44	0.989
METLL1	SRI	0.989
METLL1	NOTUM	0.988
METLL1	SLC9A1	0.988
METLL1	PGK1	0.988
METLL1	LEMD1	0.987
METLL1	NDUFS8	0.987
METLL1	WDR74	0.987
METLL1	FAM83D	0.986
METLL1	ZNF341	0.986
METLL1	POLG	0.985
METLL1	SH2B1	0.984
METLL1	C11orf68	0.98
METLL1	LARP1	0.977
METLL1	TTI2	0.975
METLL1	POLDIP3	0.971
METLL1	CCDC200	0.968
METLL1	TBCB	0.964
METLL1	LRP5	0.959
METLL1	PTK6	0.954
METLL1	SIRT4	0.945
METLL1	RAB27A	0.898
METLL1	MTRNR2L1	0.893
METLL1	ZFPM1	0.861
METLL1	UCKL1	0.847
METLL1	SCIMP	0.845
METLL1	KIF2C	0.845
METLL1	FOXJ1	0.835
METLL1	NEU1	0.834
METLL1	ATN1	0.826
METLL1	ZFAND2A	0.816
METLL1	PARP16	0.814
METLL1	TMEM107	0.812
METLL1	SEMA6A	0.795
METLL1	RGS3	0.785
METLL1	OVOL3	0.781
METLL1	LY6G6F	0.778
METLL1	LY6G6F-LY6G6D	0.778
METLL1	LOC107986004	0.772
METLL1	CNOT3	0.76

(*continued on next page*)

Table 7 (*continued*)

TF	Gene	Score
METLL1	C16orf90	0.742
METLL1	ANKRD39	0.739
METLL1	PPARD	0.731
METLL1	ABCC1	0.724
METLL1	GUCD1	0.721
METLL1	ABCA4	0.71
METLL1	TMEM262	0.707
METLL1	ARID3B	0.703
METLL1	FGG	0.702
METLL1	SNRPD3	0.696
METLL1	ZDHHC18	0.692
METLL1	SEMA4C	0.685
METLL1	PTF1A	0.683
METLL1	CLPTM1L	0.674
METLL1	SOCS2	0.669
METLL1	SREBF1	0.655
METLL1	LMNB2	0.65
METLL1	ANKRD35	0.647
METLL1	PRR14	0.647
METLL1	RPL26	0.643
METLL1	ACSL4	0.62
METLL1	USP48	0.617
METLL1	ECM1	0.591
METLL1	NEU4	0.59
NGF	ANTKMT	7.618
NGF	METRN	7.608
NGF	CCDC78	7.085
NGF	LFNG	7.027
NGF	EFNA4	6.879
NGF	NEMP1	6.673
NGF	HAGHL	6.654
NGF	ZBTB42	6.594
NGF	PAQR4	6.577
NGF	EFNA3	6.555
NGF	FBXL16	6.553
NGF	NAB2	6.514
NGF	KISS1R	6.479
NGF	R3HDM4	6.36
NGF	AKT1	6.24
NGF	SYTL1	6.211
NGF	SH2B2	6.209
NGF	NR1D1	6.18
NGF	CALR	6.143
NGF	GADD45B	6.138
NGF	KREMEN2	6.116
NGF	FIS1	6.101
NGF	PHYHIP	6.077
NGF	PCNX3	6.07
NGF	MAP3K11	6.069
NGF	ARID3A	6.051
NGF	KIAA1522	6.046
NGF	PPP1R14B	6.019
NGF	CHD4	5.991
NGF	FKBP2	5.982
NGF	FNDC11	5.965
NGF	RAD23A	5.959
NGF	ABCB9	5.953
NGF	OGFOD2	5.952
NGF	LOC114841035	5.948
NGF	TAS1R3	5.943
NGF	PKMYT1	5.935
NGF	TAPBP	5.918
NGF	RNF224	5.905
NGF	PTH2	5.873
NGF	NFIC	5.872
NGF	LRRC71	5.855
NGF	RILP	5.852
NGF	CISH	5.83
NGF	SHMT2	5.827
NGF	MAPKAPK3	5.827
NGF	SCARF1	5.817
NGF	CYSRT1	5.815
NGF	MAPK12	5.811
NGF	GFY	5.81
NGF	FARSA	5.766

Table 7 (*continued*)

TF	Gene	Score
NGF	SLC34A3	5.758
NGF	RNF208	5.739
NGF	LOC112267874	5.729
NGF	ZBTB22	5.727
NGF	ADAM15	5.698
NGF	TTC9B	5.682
NGF	KCNN1	5.669
NGF	INTS11	5.661
NGF	CPTP	5.66
NGF	CLCF1	5.645
NGF	SLC38A3	5.645
NGF	AGPAT2	5.635
NGF	ARL6IP4	5.634
NGF	SP2	5.629
NGF	OAZ1	5.624
NGF	REXO1	5.623
NGF	SERTAD1	5.619
NGF	NOS3	5.617
NGF	SERPINE1	5.611
NGF	NENF	5.603
NGF	CLDN15	5.599
NGF	HOXB4	5.598
NGF	WDR24	5.595
NGF	VASP	5.592
NGF	LBHD1	5.578
NGF	UQCC3	5.577
NGF	MAPK11	5.575
NGF	PDE4A	5.573
NGF	SLC37A4	5.558
NGF	GFER	5.535
NGF	NKX2-2	5.533
NGF	MAPK7	5.531
NGF	EHD2	5.524
NGF	NOXO1	5.521
NGF	B9D1	5.515
NGF	SRMS	5.501
NGF	PLCB3	5.497
NGF	GADD45GIP1	5.492
NGF	ARHGAP45	5.464
NGF	UCKL1	5.455
NGF	KCNK7	5.447
NGF	PLEC	5.439
NGF	PRKAR1B	5.437
NGF	SLC12A5	5.426
NGF	ELFN1	5.416
NGF	CLDN9	5.41
NGF	SPINT2	5.409
NGF	SECTM1	5.409
NGF	NEUROG2	5.401
NGF	CHTF18	3.653
NGF	TRIM39	3.306
NGF	KRT17	1.777
NGF	PGF	1.479
NGF	FOXJ1	1.431
NGF	KNTC1	1.3
NGF	F2R	1.202
NGF	POLR3G	1.012
POLR3G	HMGN4	4.191
POLR3G	ALOXE3	3.96
POLR3G	HES7	3.844
POLR3G	TRIM7	3.068
POLR3G	SHF	2.792
POLR3G	TRIM41	2.5
POLR3G	ANG	2.233
POLR3G	RNASE4	2.175
POLR3G	BORCS6	1.997
POLR3G	PGBD2	1.959
POLR3G	ZNF184	1.944
POLR3G	AGBL5	1.941
POLR3G	TRIM55	1.933
POLR3G	HSPA6	1.93
POLR3G	DPP9	1.926
POLR3G	POLR3E	1.908
POLR3G	LOC105375107	1.759
POLR3G	POM121L2	1.755

Table 7 (*continued*)

TF	Gene	Score
POLR3G	PLXDC1	1.678
POLR3G	ABT1	1.652
POLR3G	OR6S1	1.606
POLR3G	UBC	1.598
POLR3G	H4C8	1.553
POLR3G	AURKB	1.529
POLR3G	PER1	1.471
POLR3G	LASP1	1.429
POLR3G	TRIM27	1.36
POLR3G	HJV	1.349
POLR3G	TMEM107	1.284
POLR3G	PRSS16	1.28
POLR3G	MPZL1	1.245
POLR3G	H2BC17	1.05
POLR3G	MDM4	1.032
POLR3G	H2AC17	1.032
POLR3G	OR2B2	1.026
POLR3G	VAMP2	1.025
POLR3G	CGB2	0.994
POLR3G	KNL1	0.991
POLR3G	TIA1	0.986
POLR3G	ILF2	0.983
POLR3G	PLEKHG2	0.982
POLR3G	FBXO31	0.98
POLR3G	DCT	0.98
POLR3G	POLG	0.979
POLR3G	SACM1L	0.978
POLR3G	PRMT5	0.978
POLR3G	CCDC107	0.977
POLR3G	LUC7L2	0.975
POLR3G	RAB11A	0.974
POLR3G	BCAR3	0.974
POLR3G	METTL26	0.973
POLR3G	FMC1-LUC7L2	0.972
POLR3G	NDUFS7	0.972
POLR3G	LTA4H	0.97
POLR3G	TMEM259	0.969
POLR3G	SLC27A4	0.968
POLR3G	C8orf37	0.966
POLR3G	B4GAT1	0.965
POLR3G	PPP6R3	0.962
POLR3G	FMC1	0.959
POLR3G	FCGR3A	0.958
POLR3G	NCOA7	0.956
POLR3G	RPL23	0.955
POLR3G	SMARCC2	0.941
POLR3G	PPEF1	0.936
POLR3G	MYNN	0.921
POLR3G	ZMAT2	0.916
POLR3G	H2BC13	0.905
POLR3G	ZNF213	0.903
POLR3G	TMPO	0.891
POLR3G	MTRNR2L1	0.888
POLR3G	H2AC13	0.888
POLR3G	H3C12	0.875
POLR3G	ARL5C	0.872
POLR3G	PIK3C2B	0.87
POLR3G	ACTRT3	0.832
POLR3G	RNASE12	0.827
POLR3G	RS1	0.821
POLR3G	BRMS1	0.811
POLR3G	KRBA1	0.808
POLR3G	FCGR3B	0.806
POLR3G	RNASE11	0.795
POLR3G	TMEM214	0.789
POLR3G	H3C10	0.781
POLR3G	LOC101929805	0.742
POLR3G	ZNF692	0.722
POLR3G	C1QTNF6	0.719
POLR3G	PSMA3	0.713
POLR3G	CCDC115	0.709
POLR3G	CNN2	0.707
POLR3G	IMP4	0.705
POLR3G	MCRIP2	0.704

(*continued on next page*)

Table 7 (*continued*)

TF	Gene	Score
POLR3G	OR1F1	0.7
POLR3G	CGB1	0.7
POLR3G	ZFP36	0.685
POLR3G	PLLP	0.678
POLR3G	PFAS	0.674
POLR3G	WFIKKN1	0.67
POLR3G	CTC1	0.653
POLR3G	H2BC10	0.652
SVIL	H4C2	1.915
SVIL	H3C6	1.817
SVIL	H2BC8	1.813
SVIL	H3C1	1.805
SVIL	H2AC8	1.804
SVIL	H4C1	1.795
SVIL	PGBD3	1.77
SVIL	H2AC12	1.58
SVIL	H4C9	1.58
SVIL	H2BC12	1.574
SVIL	H3C2	1.569
SVIL	H1-1	1.504
SVIL	H2AC4	1.498
SVIL	H3C3	1.482
SVIL	H2BC3	1.427
SVIL	H4C4	1.375
SVIL	H2AC6	1.356
SVIL	H2BC9	1.355
SVIL	CROCC	1.355
SVIL	H2BC4	1.342
SVIL	H3C7	1.298
SVIL	H4C3	1.288
SVIL	TMEM135	1.263
SVIL	H2BC5	1.259
SVIL	LUC7L2	1.25
SVIL	FMC1-LUC7L2	1.244
SVIL	FMC1	1.234
SVIL	H1-3	1.178
SVIL	GEMIN6	1.155
SVIL	H4C7	1.153
SVIL	SRSF7	1.153
SVIL	H1-4	1.142
SVIL	H1-6	1.137
SVIL	TEX14	1.135
SVIL	MAK16	1.131
SVIL	H4C8	1.12
SVIL	TTI2	1.119
SVIL	H4C5	1.104
SVIL	TNFRSF10D	1.088
SVIL	H4C6	1.073
SVIL	TIMM13	1.06
SVIL	H2BC6	1.054
SVIL	H3C4	1.053
SVIL	H2AC7	1.053
SVIL	H2BC7	1.052
SVIL	CSDE1	1.052
SVIL	NRAS	1.044
SVIL	TET1	1.031
SVIL	CUEDC2	1.031
SVIL	H2AC11	1.027
SVIL	ZSCAN12	1.025
SVIL	ALOXE3	1.022
SVIL	FRG1	1.012
SVIL	RPS27L	1.011
SVIL	H2BC11	1.01
SVIL	PSMB6	1.009
SVIL	COA6	1.009
SVIL	EIF3E	1.008
SVIL	DSTYK	1.007
SVIL	MRPS35	1.005
SVIL	MCOLN1	1.004
SVIL	COX7A2	1.003
SVIL	FBXW9	1.001
SVIL	IST1	1
SVIL	ACCS	1
SVIL	HSP90AB1	1

(*continued on next page*)

Table 7 (*continued*)

TF	Gene	Score
SVIL	ANAPC15	1
SVIL	UBB	1
SVIL	LRRC63	1
SVIL	JMJD1C	1
SVIL	PHB	1
SVIL	EPG5	1
SVIL	FUS	1
SVIL	PSMC2	1
SVIL	SYNPO2	1
SVIL	MNAT1	0.999
SVIL	GOSR1	0.999
SVIL	ITPR1	0.999
SVIL	TDG	0.999
SVIL	FBXW7	0.999
SVIL	EEF1A1	0.999
SVIL	MTERF1	0.999
SVIL	SF3A3	0.999
SVIL	RABGAP1L	0.999
SVIL	NDUFAF1	0.999
SVIL	RPL12	0.999
SVIL	NSL1	0.999
SVIL	JUNB	0.999
SVIL	COX14	0.999
SVIL	LRRC37A3	0.999
SVIL	EMC4	0.999
SVIL	HNRNPA2B1	0.999
SVIL	RPL7	0.999
SVIL	RPS27	0.999
SVIL	RPL10	0.998
SVIL	HSPA1A	0.998
SVIL	DVL2	0.998
SVIL	RPS6	0.998
SVIL	MAGED1	0.998
SVIL	ZNHIT6	0.998
TOE1	LOC101929601	3.499
TOE1	LOC101929627	3.235
TOE1	ZDHHC7	2.861
TOE1	RASA4	2.803
TOE1	ARID1A	2.729
TOE1	PPP2R5B	2.595
TOE1	ATG2A	2.582
TOE1	MNT	2.545
TOE1	MRPL48	2.493
TOE1	MCRIP2	2.47
TOE1	H2AX	2.433
TOE1	TSEN34	2.422
TOE1	MBOAT7	2.407
TOE1	MFAP3L	2.379
TOE1	MRPL44	2.347
TOE1	WDR90	2.338
TOE1	MRPL40	2.333
TOE1	HIRA	2.314
TOE1	DPAGT1	2.295
TOE1	EIF2B5	2.221
TOE1	METTL26	2.206
TOE1	FGF9	2.193
TOE1	RGL2	2.168
TOE1	PYGO2	2.164
TOE1	HMBS	2.156
TOE1	LOC101928120	2.155
TOE1	PBXIP1	2.141
TOE1	RTEL1	2.131
TOE1	SLC25A39	2.103
TOE1	VILL	2.095
TOE1	NEU1	2.091
TOE1	TRIP6	2.088
TOE1	LOC107985728	2.088
TOE1	AMDHD2	2.084
TOE1	FZR1	2.072
TOE1	KIAA0513	2.029
TOE1	ACAP2	2.022
TOE1	SYTL1	2.017
TOE1	FUT1	2.014
TOE1	KIAA0586	2.01
TOE1	TIMM9	2.01

Table 7 (*continued*)

TF	Gene	Score
TOE1	GOLGA6L10	2.01
TOE1	CAMK1	1.993
TOE1	SAMD11	1.992
TOE1	UBC	1.986
TOE1	NOTCH2NLA	1.977
TOE1	RAB7A	1.973
TOE1	C4orf47	1.97
TOE1	UFSP2	1.97
TOE1	AP3S1	1.961
TOE1	MCEE	1.961
TOE1	TMEM250	1.959
TOE1	LRRC1	1.958
TOE1	P3H4	1.958
TOE1	KCNAB2	1.956
TOE1	NPHP4	1.956
TOE1	RBPJ	1.955
TOE1	MPHOSPH10	1.952
TOE1	RAP2B	1.951
TOE1	DNAAF3	1.95
TOE1	MRPL36	1.948
TOE1	DOHH	1.947
TOE1	ERAP1	1.947
TOE1	RPS9	1.943
TOE1	SEPTIN2	1.941
TOE1	CITED2	1.941
TOE1	HDLBP	1.94
TOE1	ATG12	1.94
TOE1	ZFAND6	1.937
TOE1	TDP1	1.936
TOE1	LNPEP	1.935
TOE1	FAM72D	1.931
TOE1	ZFP91	1.926
TOE1	ATP6V0C	1.922
TOE1	EEF2	1.922
TOE1	TRIM65	1.919
TOE1	CCNT2	1.918
TOE1	C2	1.918
TOE1	EHMT2	1.918
TOE1	EFCAB11	1.916
TOE1	GANAB	1.916
TOE1	ISOC2	1.914
TOE1	ANP32B	1.914
TOE1	SLC12A9	1.913
TOE1	COMMD1	1.913
TOE1	NACC1	1.912
TOE1	YPEL5	1.911
TOE1	TRMT1	1.91
TOE1	FKBP10	1.906
TOE1	HSPG2	1.905
TOE1	INTS5	1.902
TOE1	ZMIZ1	1.901
TOE1	ARL5A	1.9
TOE1	PLEKHA8	1.897
TOE1	COIL	1.896
TOE1	MEIS1	1.894
TOE1	SRRT	1.892
TOE1	GATD3B	1.89
TOE1	FKBP14	1.885
TOE1	SRGAP2B	1.883
TRIM3	Pde2a	4.206
TRIM3	Ptp4a3	4.194
TRIM3	Erg	4.052
TRIM3	Cxxc5	3.926
TRIM3	Rassf2	3.738
TRIM3	Chrna9	3.689
TRIM3	LOC115488942	3.652
TRIM3	Cbfa2t3	3.558
TRIM3	Cep250	3.508
TRIM3	Dnah7a	3.483
TRIM3	Cerk	3.431
TRIM3	Rac2	3.411
TRIM3	Plxnd1	3.384
TRIM3	Zbtb18	3.369
TRIM3	Laptm5	3.32
TRIM3	Adssl1	3.316

Table 7 (*continued*)

TF	Gene	Score
TRIM3	Pomgnt2	3.221
TRIM3	N4bp3	3.216
TRIM3	Smad3	3.206
TRIM3	Rmnd5b	3.195
TRIM3	Iqcn	3.182
TRIM3	Cd52	3.168
TRIM3	Cyth4	3.162
TRIM3	Jund	3.161
TRIM3	Unc93b1	3.117
TRIM3	Tfap4	3.098
TRIM3	Sfi1	3.093
TRIM3	Ttpal	3.091
TRIM3	Tpcn1	3.09
TRIM3	Eef2k	3.078
TRIM3	Aldh3b1	3.075
TRIM3	Gm4832	3.061
TRIM3	Adgre5	2.984
TRIM3	Il2ra	2.932
TRIM3	Fmnl1	2.896
TRIM3	Tfeb	2.886
TRIM3	Wdfy4	2.886
TRIM3	Slamf6	2.88
TRIM3	Gm32211	2.862
TRIM3	Ddit4	2.849
TRIM3	Abca6	2.843
TRIM3	Aff1	2.837
TRIM3	Tpst2	2.816
TRIM3	Ky	2.815
TRIM3	Lrmp	2.787
TRIM3	Srl	2.77
TRIM3	Irgc1	2.761
TRIM3	Ralgds	2.76
TRIM3	Al467606	2.756
TRIM3	Ubxn11	2.733
TRIM3	Pacsin1	2.732
TRIM3	Snn	2.707
TRIM3	Ackr2	2.699
TRIM3	Ppp1r18	2.686
TRIM3	Msh6	2.664
TRIM3	Akna	2.662
TRIM3	Rgs8	2.657
TRIM3	Hdac7	2.647
TRIM3	Emid1	2.628
TRIM3	Fam129c	2.613
TRIM3	Fgd2	2.599
TRIM3	4930467E23Rik	2.598
TRIM3	Gna15	2.598
TRIM3	Rilpl2	2.572
TRIM3	Inf2	2.569
TRIM3	Pxdn	2.567
TRIM3	Scgb1a1	2.549
TRIM3	Gm19402	2.546
TRIM3	Amz2	2.529
TRIM3	H4c14	2.525
TRIM3	Cyth1	2.518
TRIM3	Nr4a1	2.509
TRIM3	Kcnj12	2.496
TRIM3	Cxcr4	2.495
TRIM3	Pxn	2.491
TRIM3	Dgkd	2.489
TRIM3	Enpp6	2.479
TRIM3	Cd79b	2.475
TRIM3	Sike1	2.471
TRIM3	Cdh17	2.434
TRIM3	Nmrk1	2.427
TRIM3	Rbm17	2.421
TRIM3	Arap1	2.42
TRIM3	Ostf1	2.414
TRIM3	Tspear	2.414
TRIM3	P2rx1	2.398
TRIM3	Rnase10	2.394
TRIM3	BC034090	2.387
TRIM3	Tex14	2.381
TRIM3	Ech1	2.378
TRIM3	Bex6	2.378

(*continued on next page*)

Table 7 (*continued*)

TF	Gene	Score
TRIM3	Asb2	2.373
TRIM3	Rbm38	2.373
TRIM3	Socs3	2.37
TRIM3	Cnn1	2.363
TRIM3	Pgls	2.362
TRIM3	Kcnab2	2.361
TRIM3	Stambpl1	2.357
TRIM3	Lrrc32	2.348
TRIM3	Nrm	2.344

incubated for 2 h in an incubator at 37 °C, DAPI dye solution was added, the slides were incubated for 10 min at room temperature in the dark, and the slides were sealed with anti-fluorescence quenching tablet sealing agent. Microscopic photography: Sections were observed under a fluorescence microscope, and images were collected. DAPI emits blue light at 420 nm, while CY3 emits red light at 590 nm.

3.14. Observation of the cell substructure by fluoroscopic electron microscopy

TECs were collected, digested with 0.25% trypsin and made into a cell suspension. After washing with PBS, the cell precipitate was centrifuged and fixed for 4 h. After immersion in acetone, ultrathin sections of 80 nm were stained with uranium and lead, observed under a transmission electron microscope (Hitachi, HT7700), and photographed for image analysis.

3.15. Continuous observation of the morphology of cocultured TECs by a Nanolive 4D microscope

P4 generation TECs at a cell concentration of 5000/ml were added to a Nanolive 4D microscope petri dish, and then 1.5 ml DMEM/F12 (containing 10% fetal bovine serum) medium was added and mixed slowly; the medium was discarded after 24 h of culture. Then, DMEM/F12 containing 200 μmol/L H_2O_2 was added to treat the TECs for 72 h, after which the medium was discarded. Next MSCs at a P4 generation cell concentration of 5000 cells/ml were added and incubated for 48 h The Nanolive 4D microscope (Nikon Eclipse C1) was started and connected to the computer, the focal length was adjusted to take pictures under the appropriate field of vision for 48 h, and pictures were taken every 4 min.

3.16. DNA methylation and transcriptome sequencing

The TECs of MSCs were 1.3×10^7 in coculture and 1.2×107 in the induced senescence group. The cell precipitates were frozen in liquid nitrogen and stored at −80 °C for 24 h. Whole-genome methylation and transcriptome data were obtained by whole-genome methylation and transcriptome sequencing at Guangzhou Jidiao Biotechnology Co., Ltd (2009).

3.17. Analysis of DNA methylation sequencing data

The obtained clean data were mapped to the species reference genome using BSMAP software (version 2.90). The methylated cytosine level was then detected using a custom Perl script and assessed using the correction algorithm described by Lister R et al. The level of methylation was calculated based on the percentage of methylation of each sequence (CG, CHG, and CHH) in the entire genome, each chromosome, and different regions of the genome. To explain the changes in DNA methylation in TECs, methylation maps

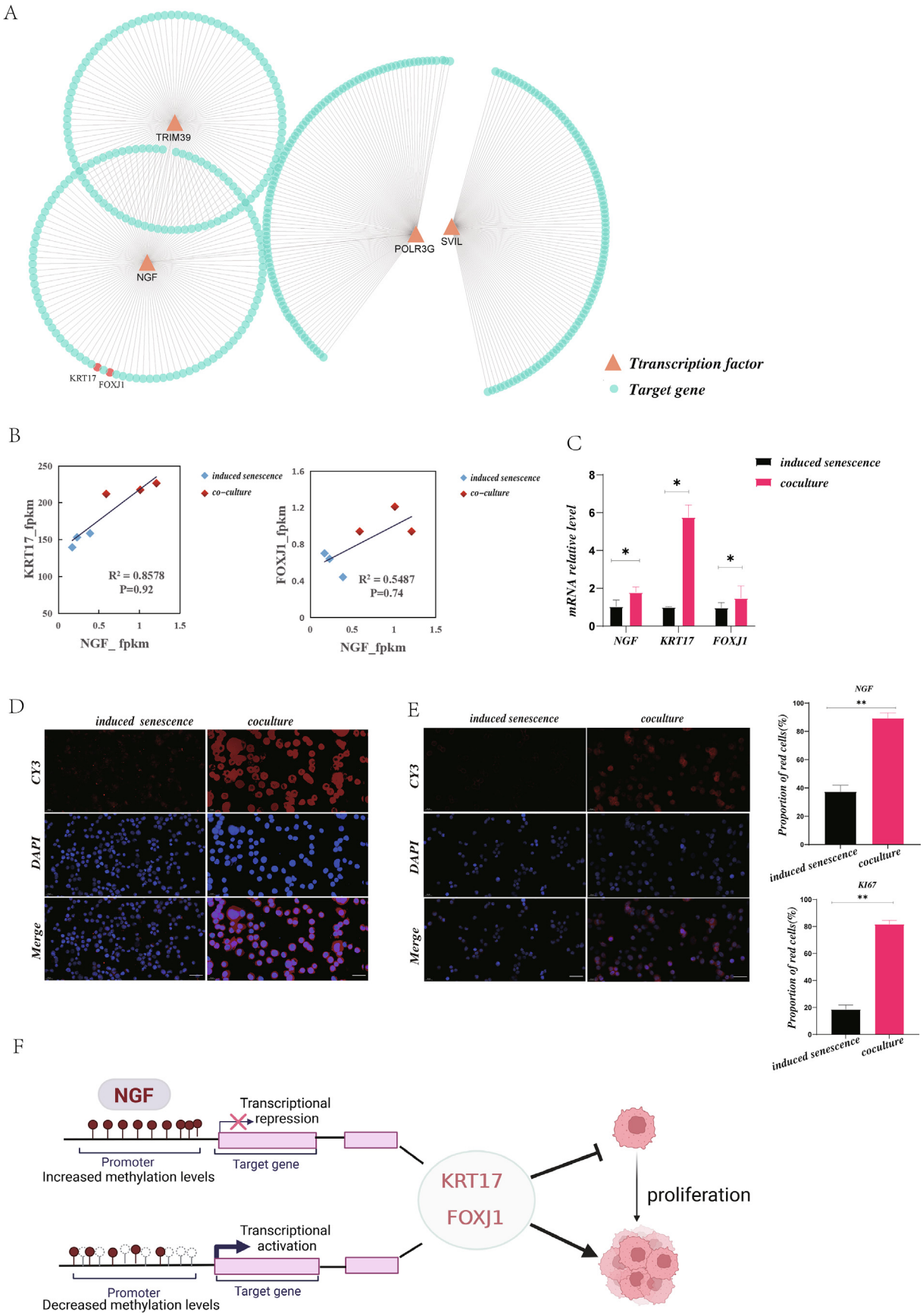

Fig. 5. MSCs induce NGF demethylation to regulate the expression of KRT17 and FOXJ1. **A** MSCs reverse the methylation of transcription factors and the regulatory network of target genes during TEC aging (orange triangles represent transcription factors, and blue circles represent target genes). **B** The transcription factor NGF was associated with the RNA-seq expression of the target genes KRT17 and FOXJ1 during the reversal of TEC senescence by MSCs. The horizontal coordinate represents the expression of the transcription factor NGF,

of the upstream 1 kb region and gene body were drawn according to the average methylation level of each window. Changes in GC content were screened according to the number of differentially methylated regions (DMRs) (≥5) and the absolute value of methylation ratio difference (≥0.1). The senescence genes were counted according to Gene Ontology Consortium.

3.18. RNA-seq analysis

The transcriptome database was analyzed by DESeq2 software, and the mRNAs satisfying the conditions of log2FC > 1.2 and P value < 0.05 were regarded as differentially expressed genes. The differentially expressed genes in ageing TECs and ageing TECs after coculture were counted and analyzed by gene function annotation.

3.19. Analysis of the relationship between gene methylation and transcriptional level

To calculate the correlation between gene methylation and transcription, the genes were divided into four groups according to the transcription level in RNA-seq data (FPKM ≤1 for no transcription, 1 < FPKM ≤10 for low transcription, 10 < FPKM ≤100 for medium transcription and FPKM >100 for high transcription). The Pearson correlation coefficients between upstream/gene body methylation levels and corresponding gene expression levels in TECs of the control, model and coculture groups were calculated.

3.20. Establishment of the transcription factor-methylation regulatory network

To explore the relationship between specific gene methylation and transcription factor binding, the TFs of ageing-related genes were predicted by CistromeDB, and the TF-DNA regulatory network was constructed by Cytoscape.

3.21. Enrichment analysis

Through the Gene Ontology database (GO item in http://www.geneontology.org/)), the number of genes in each item was calculated, and the GO items significantly enriched relative to the genomic background were defined by hypergeometric test. KEGG is the main public pathway-related database (http://www.kegg.jp/kegg/)).

3.22. Functional verification

3.22.1. Expression analysis of RAP1 signal pathway molecules RAP1, SRC and ITGB3

For Western blotting analysis, the primary anti-rabbit anti-human RAP1 (1RV 1000, ab14404), SRC (1RV 30000 ab179473 ab109381) and ITGB3 (1RV 1000 ab179473) were all obtained from Abcam, as described above.

3.22.2. Analysis of the relative expression of the ageing regulatory genes NGF, KRT17 and FOXJ1

Total RNA was extracted according to the production manual (Carlsbad Invitrogen Company, California) by RT-QPCR using TRIzol reagent. cDNA was amplified by reverse transcriptase (GoldenstarTM RT6, China) and random primers. According to the SYBR Green Master Mix specification (TsingKe Biotech Co., China), a CFX96TM Real-Time System (Applied 2720) was used for qPCR. The glyceraldehyde 3-phosphate dehydrogenase (GAPDH) gene was used as an internal control. Each experiment was repeated 3 times, and the gene expression level was normalized by the 2-T square method. All qPCR primers are listed in (Supplementary Table 1).

3.22.3. For immunofluorescence detection of NGF and KI67 expression

TECs were collected and fixed with paraformaldehyde, and the fixation solution was removed. Anti-mouse anti-human antibodies against Ki67 and NGF (1R1000 ~ (th) ServiceBio) were added for staining. The nuclei at 15 min were restrained with CY3 goat anti-rabbit DAPI at room temperature for 50 min and then sealed with anti-fluorescence quenching sealant. Microscopic examination: The sections were observed under a fluorescence microscope, and images were collected (Nikon DS-U3, Nikon, Japan; DAPI UV excitation wavelength 380 nm, emission wavelength 420 nm, blue light; CY3 excitation wavelength 510–560 nm, emission wavelength 590 nm, red light). The number of positive cells was analyzed by ImageJ software (NIH, Bethesda, MD).

3.23. Statistical analysis

SPSS 21.0 statistical software was used for analysis, and the data are expressed as the mean ± standard deviation. A *t*-test was used to compare the two groups, and one-way analysis of variance (one-way ANOVA) was used to analyze the significance of differences among the three groups.

4. Discussion

Thymus aging weakens the immune system and other functions of the human body and is a progressive, multifactorial and complex biological process caused by serious damage to the microenvironment and integrity of the thymus matrix. MSC transplantation, as a new method for the treatment of thymus aging, has been proven to be effective and safe, and it has been proposed as a treatment to restore the structure and function of the thymus; for example, MSCs significantly increase the thymus index and improve the histological structure of the aging thymus [14]. Similarly, the structure was reconstructed, and the function of the aging thymus was improved after continuous MSC infusion [20]. However, in-depth research on this process in primates is lacking. Interestingly, we found that MSCs could regulate DNA methylation profiles to promote the division and proliferation of aging TECs, thereby improving the structure and function of the thymus in aging macaques.

Rhesus monkey belongs to non-human primates, whose genome sequencing is 93% similar to human genome, and the research results are more valuable for reference than other animals. In this study, we used elderly rhesus monkeys as a model to observe the effect of MSCs on thymus structure and function. To our surprise, our results showed that the volume of the thymus increased, the number of thymus lobules increased, the number of thymus epithelial cells and thymocytes increased, and the number of Hassall bodies and the amount of adipose tissue decreased. Moreover, the thymus index and the levels of thymosin α and thymopoietin in peripheral blood were decreased, the aging marker gene P16 was downregulated, and the TEC marker molecule CK14+ was upregulated after MSC treatment. These results implied that MSC treatment improved the structure and function of the thymus and promoted the regeneration of the thymic lobules.

and the ordinate represents the expression of the target gene. **C** The mRNA expression levels of demethylated NGF, KRT17 and FOXJ1 were analyzed via qPCR. **D** The expression of NGF was detected by immunofluorescence (400×). **E** The expression of the TEC proliferation marker Ki67 was detected by immunofluorescence (400×). **F** Regulatory role of decreased methylation of the NGF/KRT17/FOXJ1 axis in the MSC-mediated reversal of TEC senescence. The measured values represent the mean ± standard deviation ($\bar{X} \pm s$) of three replicate experiments. *P < 0.05, **P < 0.01, ***P < 0.001).

The current consensus is that the therapeutic mechanism of MSCs involves its homing and strong paracrine functions [21,22]. Our results were consistent with previous studies showing that MSCs promote thymus regeneration by secreting various cytokines or differentiating into thymus tissue cells [23,24]. The above results suggest that MSC treatment improves the structure and function of the thymus in elderly rhesus monkeys.

As TECs are among the most important supporting cells of the thymus, their activity and quantity are crucial to the structural maintenance and function of this organ [25]. Therefore, we used human TECs as the research object, induced aging by H_2O_2, and observed the effect of intervention with MSCs. H_2O_2 is a small molecule that induce cell senescence due to oxidative stress caused by high levels of free radicals produced by the cell membrane, and increase the activity of SA-β-gal and expression of P16 and P21 [26–28], which were consisted with our results that the changes of TECs after treatment with 200 μmol/L H_2O_2 for 72 h. Interestingly, when senescent TECs were cocultured with MSCs in Transwell chambers for 48 h, the activity of SA-β-gal decreased, and P16 and P21 down-regulated, chromatin was evenly distributed, and autophagosomes were observed. Moreover, under a Nanolive 4D microscope, it was found that MSCs continuously secreted vesicular substances into ageing TECs, resulting in uniform distribution of TEC chromatin, appearance of intracellular autophagosomes and smaller cell morphology. These results suggested that MSCs would secrete vesicular substances improve the structure, and down-regulate ageing relative markers to reverse the ageing TECs.

DNA methylation plays an important role in regulating cell structure and function, but whether MSCs regulate DNA methylation to promote the division and proliferation of TECs has not been studied in depth [29,30]. Based on the analysis of the results of genome-wide methylation sequencing, it was found that the sites of methylation modification were mainly concentrated in CG loci, which was consistent with reports in mammals [31]. Then, we analyzed the methylation level of different positions of the gene and observed significant hypomethylation around the transcriptional start site, results showed that the methylation level of the gene body was higher than that of the adjacent region, and the methylation level decreased significantly after the transcriptional end site, indicating that the methylation level changed differently at different locations of the gene [32,33]. In addition, The results of differential methylation gene analysis between groups showed that 23 genes that inhibited cell growth and proliferation were methylated, and 37 genes that promoted cell growth and anti-inflammatory and antioxidant stress were demethylated in TECs after MSCs coculture, which indicated that methylation in the promoter region is one of the key mechanisms by which MSCs reverse TEC senescence.

It has been confirmed that DNA methylation in the gene promoter region can lead to gene silencing [32]. Our study revealed that the methylation of the ageing-promoting genes PDE5A, DUOX2, LAMP1 and SVIL in the promoter region leads to a decrease in the transcription level, while a decrease in the methylation level of the growth-promoting genes POLR3G, PGF, CHTF18, KRT17, FOXJ1, NGF, DYRK3, LRP8, CDT1, PRELID1, F2R, KNTC1 and TRIM3 leads to an increase in the transcription level. The Rap1 signaling pathway plays an important role in cell adhesion and integrin function in many cell types [34]. After coculture with MSCs, it activates the Rap1 signaling pathway, increases the expression of Rap1, SRC and ITGB3, promotes cell proliferation and facilitates resistance to apoptosis [35–37]. In the gene body region, although some studies have confirmed the effect of gene body DNA methylation on gene expression, the function of gene body DNA methylation is still poorly understood [38,39]. In our study, MSCs in the gene body region not only inhibited gene transcription but also promoted the transcription of some genes in the process of reversing TEC ageing.

DNA methylation in the promoter region prevents binding to transcription factors, leading to gene silencing [40]. Our research shows that NGF gene methylation inhibits the expression of KRT17 and FOXJ1, which highlights the regulatory mechanism of DNA methylation in the process of MSCs coculture with senescent TECs. Nerve growth factor NGF is reported to exist mainly in medullary epithelial cells of normal and regenerated thymic Hassall bodies, stimulating the activity and proliferation of mouse TECs in vitro [41,42]. Therefore, NGF may be a candidate regulatory gene in the process of MSCs coculture of ageing TECs. In addition, KRT17 and FOXJ1, as downstream regulators of NGF, are involved in epithelial cell development, but no studies describing the effects of these genes on TEC senescence have been published, so they may be new markers of TEC cell adhesion, cell proliferation and tissue development.

5. Conclusion

MSCtreatment significantly improved the morphology and structure of the thymus, reduced the expression level of aging markers, and promoted the activity of aging TECs to improve thymus structure and function. The mechanism by which MSCs promote thymus regeneration involves inhibition of the expression of senescence genes by inducing methylation in the promoter region of aging-related genes and inhibiting promoter methylation in cell growth- and differentiation-related genes to regulate their expression. Furthermore, MSCs upregulate KRT17 and FOXJ1 by increasing the expression of genes related to the RAP1 signaling pathway and regulate the demethylation of NGF genes to promote the proliferation of TECs.

Ethics approval and consent to participate

All experimental protocols were approved by the relevant committees of the 920th Hospital of the Joint Logistics Support Force of the Chinese People's Liberation Army.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analyzed during this study are included in this published article. The datasets [GENERATED/ANALYZED] for this study can be found in the [https://www.jianguoyun.com/p/DTP_bNkQgbjoCxj36ZMFIAA] and GSA -gsa-human (HRA005210).

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Authors' contributions

XHP and XJW designed the study. ZLY, TC, XQZ, HJ, PH, LY, GPR performed the experiments and collected the data. ZLY wrote the manuscript. TC and ZXH assisted with the literature searches and

revised the manuscript. All authors read and approved the final manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.reth.2024.03.008.

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