Table E1. Differentially expressed genes between cultured primary nasal epithelial cells and NE

Chromosome	Gene.Name	Gene.ID	Sum.of.Exon.Length.of.Gene
chr12	KRT6A	ENSG00000205420	2489
chr17	KRT17	ENSG00000128422	2460
chr12	KRT6C	ENSG00000170465	2813
chr1	S100A2	ENSG00000196754	1567
chr1	S100A9	ENSG00000163220	577
chr17	KRT14	ENSG00000186847	2251
chr1	LAMB3	ENSG00000196878	4628
chr1	SFN	ENSG00000175793	1315
chr17	KRT16	ENSG00000186832	2475
chr1	S100A14	ENSG00000189334	1277
chr1	LAMC2	ENSG00000058085	6406
chr1	SPRR1B	ENSG00000169469	620
chr4	AREG	ENSG00000109321	1648
chr4	AREGB	ENSG00000205595	1647
chr1	S100A6	ENSG00000197956	774
chr16	MT2A	ENSG00000125148	903
chr19	LGALS7B	ENSG00000178934	644
chr9	ANXA2P2	ENSG00000231991	1310
chr19	LGALS7	ENSG00000205076	795
chr17	ITGB4	ENSG00000132470	6629
chr20	SLPI	ENSG00000124107	596
chr1	G0S2	ENSG00000123689	866
chr1	F3	ENSG00000117525	2875
chr13	GJB2	ENSG00000165474	2425
chr1	S100A8	ENSG00000143546	889
chr1	TACSTD2	ENSG00000184292	2068
chr17	KRT19	ENSG00000171345	1891
chr1	S100A16	ENSG00000188643	1675
chr10	COL17A1	ENSG00000065618	6426
chr1	SPRR1A	ENSG00000169474	647
chr22	LGALS1	ENSG00000100097	969
chr9	ANXA1	ENSG00000135046	4561
chr15	ANXA2	ENSG00000182718	8268
chr12	KRT7	ENSG00000135480	3884
chr12	KRT75	ENSG00000170454	2324
chr2	IL1A	ENSG00000115008	2124
chr1	S100A11	ENSG00000163191	680
chr10	ANXA8L1	ENSG00000150165	2127
chr12	RP11-1020M18.10	ENSG00000257500	629
chr10	ANXA8L2	ENSG00000186807	2128
chrX	SAT1	ENSG00000130066	2075
chr6	CDKN1A	ENSG00000124762	2933
chr12	RP11-386G11.10	ENSG00000258017	1388

Table E2. Functional anno
A. cNE> NEC-iPSC

Annotation Cluster 1
Category
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT

Annotation Cluster 2
Category
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT

Annotation Cluster 3
Category
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_CC_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT

Annotation Cluster 4
Category
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT

Annotation Cluster 5

Table E3. Differentially methylated CpG sites between cultured primary nasal epithelial cells an

TargetID	cNE_1	cNE_2	cNE_3	NEC_iPSC_1	NEC_iPSC_2	NEC_iPSC_3	meancNE
cg15835664	0.0500	0.0531	0.0508	0.8622	0.8634	0.8654	0.0513
cg07543967	0.0238	0.0189	0.0230	0.9342	0.9340	0.9304	0.0219
cg08199953	0.9207	0.9187	0.9213	0.0469	0.0458	0.0452	0.9202
cg09556700	0.0420	0.0457	0.0425	0.8997	0.9041	0.9017	0.0434
cg03370077	0.0672	0.0714	0.0690	0.8768	0.8797	0.8796	0.0692
cg06799735	0.0642	0.0664	0.0631	0.7385	0.7368	0.7406	0.0646
cg18598117	0.0093	0.0132	0.0075	0.9846	0.9786	0.9844	0.0100
cg10622644	0.0315	0.0359	0.0316	0.9048	0.9042	0.9097	0.0330
cg24697184	0.0583	0.0588	0.0594	0.3166	0.3154	0.3168	0.0588
cg05050042	0.9755	0.9790	0.9817	0.0232	0.0204	0.0183	0.9787
cg02604225	0.0469	0.0451	0.0509	0.8981	0.9009	0.9047	0.0476
cg24647820	0.0371	0.0410	0.0398	0.8426	0.8374	0.8413	0.0393
cg16072777	0.0273	0.0325	0.0283	0.8215	0.8270	0.8273	0.0294
cg13580834	0.0394	0.0383	0.0438	0.7936	0.7903	0.7949	0.0405
cg00944666	0.0910	0.0903	0.0960	0.8382	0.8437	0.8391	0.0924
cg18354462	0.0945	0.0927	0.0976	0.7723	0.7737	0.7775	0.0949
cg20850016	0.0292	0.0339	0.0312	0.6654	0.6680	0.6689	0.0314
cg22215508	0.0279	0.0268	0.0323	0.7916	0.7955	0.7956	0.0290
cg18708412	0.2119	0.2108	0.2158	0.7883	0.7925	0.7926	0.2129
cg23622047	0.0405	0.0344	0.0395	0.8824	0.8795	0.8870	0.0382
cg01697719	0.8381	0.8396	0.8450	0.0147	0.0204	0.0131	0.8409
cg05991442	0.0237	0.0155	0.0154	0.9794	0.9857	0.9794	0.0182
cg02357751	0.9775	0.9771	0.9864	0.0182	0.0255	0.0297	0.9803
cg12601118	0.0162	0.0239	0.0200	0.9727	0.9667	0.9760	0.0200
cg11452329	0.0219	0.0254	0.0319	0.9638	0.9558	0.9559	0.0264
cg09550697	0.0593	0.0628	0.0520	0.9706	0.9812	0.9770	0.0580
cg14428166	0.0371	0.0433	0.0336	0.9337	0.9314	0.9408	0.0380
cg10030684	0.0264	0.0314	0.0338	0.8710	0.8753	0.8802	0.0305
cg09445935	0.8925	0.8955	0.8932	0.0516	0.0469	0.0484	0.8938
cg20477160	0.0552	0.0478	0.0482	0.8985	0.8920	0.8949	0.0504
cg09803262	0.8920	0.8840	0.8875	0.0479	0.0488	0.0408	0.8878
cg07060794	0.0672	0.0729	0.0662	0.9089	0.9086	0.9134	0.0688
cg02579959	0.0734	0.0696	0.0765	0.8862	0.8845	0.8926	0.0731
cg01515444	0.0691	0.0614	0.0672	0.8772	0.8685	0.8752	0.0659
cg16754788	0.0892	0.0975	0.0970	0.8885	0.8962	0.8947	0.0945
cg08576476	0.0278	0.0354	0.0325	0.8272	0.8283	0.8351	0.0319
cg06481431	0.0372	0.0441	0.0444	0.8354	0.8322	0.8390	0.0419
cg21970789	0.8612	0.8562	0.8639	0.0704	0.0698	0.0632	0.8605
cg24686551	0.0399	0.0345	0.0414	0.8245	0.8193	0.8244	0.0386
cg18251389	0.0285	0.0233	0.0191	0.7779	0.7809	0.7869	0.0236
cg22540040	0.0814	0.0730	0.0774	0.8246	0.8331	0.8283	0.0773
cg12018581	0.0419	0.0404	0.0363	0.7756	0.7830	0.7782	0.0395
cg01899130	0.0503	0.0496	0.0526	0.7883	0.7890	0.7925	0.0508

Table E4. Functional clust

Annotation Cluster 1
Category
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT

Annotation Cluster 2
Category
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_MF_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT

Annotation Cluster 3
Category
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT

Annotation Cluster 4
Category
GOTERM_CC_FAT
GOTERM_CC_FAT
GOTERM_CC_FAT

Table E5. Differentially methylated CpG sites between NEC-iPSCs and ESCs.

A. All 1731 CpG sites

TargetID	meanESC	meanIPSC	meancNE	absd_ESCvsiPSC	BHp_ESCvsIPSC
cg03699469	0.4937	0.0335	0.0346	0.4601	0.0017
cg21823080	0.7828	0.0354	0.3187	0.7474	0.0074
cg12080079	0.1769	0.6571	0.5791	0.4802	0.0074
rs3936238	0.9539	0.0256	0.0284	0.9284	0.0074
cg18375421	0.8798	0.1318	0.1575	0.7481	0.0077
cg23476401	0.8713	0.4024	0.6323	0.4690	0.0077
cg13424673	0.8318	0.0447	0.0468	0.7871	0.0084
cg14670974	0.9731	0.0036	0.0086	0.9695	0.0084
cg01847719	0.9625	0.0270	0.0200	0.9355	0.0084
cg13423383	0.9135	0.0595	0.2962	0.8539	0.0084
cg00963169	0.5798	0.0198	0.0241	0.5600	0.0084
cg02623400	0.5101	0.0318	0.0467	0.4783	0.0084
cg08519216	0.6086	0.0223	0.0122	0.5863	0.0084
cg22962698	0.5023	0.0155	0.0124	0.4868	0.0084
cg03091331	0.6812	0.1130	0.1455	0.5682	0.0084
cg14189141	0.9534	0.0162	0.0228	0.9372	0.0084
rs1416770	0.9611	0.0306	0.0293	0.9306	0.0084
rs5987737	0.9515	0.0206	0.9546	0.9310	0.0084
cg14369648	0.9623	0.0237	0.0217	0.9385	0.0087
cg07883457	0.4447	0.0129	0.1870	0.4318	0.0087
cg05331731	0.3675	0.2089	0.5649	0.1585	0.0089
cg13300273	0.9810	0.0776	0.0370	0.9033	0.0089
cg24434800	0.4744	0.0447	0.0971	0.4297	0.0089
cg02469838	0.5169	0.6616	0.4611	0.1447	0.0089
cg05759718	0.9569	0.0166	0.0166	0.9402	0.0091
cg13678973	0.6333	0.0242	0.0342	0.6091	0.0091
cg05463257	0.6902	0.5394	0.6924	0.1507	0.0091
cg17641252	0.8114	0.1479	0.0320	0.6635	0.0091
cg00968488	0.0582	0.5868	0.0864	0.5286	0.0091
cg06817264	0.8437	0.4174	0.0677	0.4263	0.0094
cg16908938	0.0479	0.8851	0.1807	0.8372	0.0107
cg02086866	0.4205	0.5306	0.4441	0.1101	0.0107
cg13647892	0.0704	0.8761	0.7055	0.8057	0.0108
cg14615336	0.7911	0.0466	0.0511	0.7445	0.0122
cg19961545	0.6519	0.0371	0.0378	0.6149	0.0122
cg00397324	0.6653	0.0111	0.0053	0.6542	0.0122
cg11748936	0.4867	0.0544	0.0544	0.4323	0.0122
cg18490616	0.4884	0.0449	0.0641	0.4435	0.0122
cg18588323	0.3816	0.2632	0.0721	0.1184	0.0122
cg03217897	0.8427	0.0507	0.0532	0.7920	0.0122
cg13138089	0.7029	0.0245	0.0279	0.6784	0.0122
cg19300401	0.0384	0.9101	0.7996	0.8717	0.0122
cg04039414	0.4947	0.0235	0.0177	0.4712	0.0129

Table E6. Functional anr

A.CpG sites with potenti

Annotation Cluster 1
Category
GOTERM_MF_FAT
GOTERM_MF_FAT
GOTERM_MF_FAT
GOTERM_MF_FAT
GOTERM_MF_FAT

Annotation Cluster 2
Category
SMART
SMART
GOTERM_MF_FAT
GOTERM_MF_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_MF_FAT
GOTERM_MF_FAT

Annotation Cluster 3
Category
GOTERM_CC_FAT
GOTERM_CC_FAT
GOTERM_CC_FAT
GOTERM_CC_FAT

Annotation Cluster 4
Category
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_CC_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT

Annotation Cluster 5
Category
GOTERM_BP_FAT
GOTERM_BP_FAT
GOTERM_BP_FAT

Annotation Cluster 6
Category
GOTERM_BP_FAT

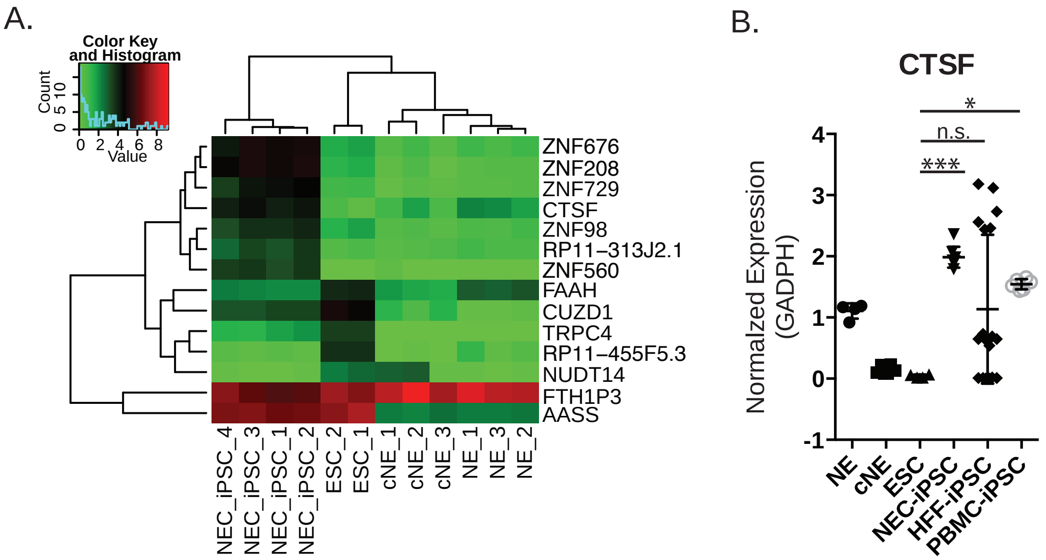
Table E7. Primers for qPCR.

Primer	Sequence
NANOG_F	5’-AAAGAATCTTCACCTATGCC-3’
NANOG_R	5’- GAAGGAAGAGGAGAGACAGT-3’
NANOG_F_2	5’- CTAAGAGGTGGCAGAAAAACA-3’
NANOG_R_2	5’- CTGGTGGTAGGAAGAGTAAAGG-3’
MEOX1_F	5’- AGGAGAGTTCAGACAACCAG-3’
MEOX1_R	5’- CGAGTCAGGTAGTTATGATGG-3’
FOXF1_F	5’- GCCTCTTATATCAAGCAGCA-3’
FOXF1_R	5’- CAAACTCCTTTCGGTCACAC-3’
ALB_F	5’- GAAGACTATCTATCCGTGGT-3’
ALB_R	5’ TCAGCATTAAACTCTTTGGG-3’
FABP1_F	5’-TTCTCCGGCAAGTACCAACT-3’
FABP1_R	5’- CACCCCCTTGATATCCTTCC-3’
SOX1_F	5’- CAAGTTGCTAACCGATGTGA-3’
SOX1_R	5’- GGAAACCTAAGGCTGCTGA-3’
TH_F	5’- GAAATTGAGAAGCTGTCCAC-3’
TH_R	5’- CTCTCAGACACGAAGTAGAC-3’
CK19_F	5’-GGTCAGTGTGGAGGTGGATT-3’
CK19_R	5’-TCAGTAACCTCGGACCTGCT-3’
CTSF_F	5’-CCTGTTGAATGAGGATCCCC-3’
CTSF_R	5’-GCTCGCACCATGTTATTGAC-3’
KRT5_F	5’-GCTGAGAATGAGTTTGTGATGC-3’
KRT5_R	5’-GCTCCGCATCAAAGAACATC-3’
SPRR2A_F	5’-ACCCCTGGTACCTGAGC-3’
SPRR2A_R	5’-TGCTGTTGATAAGACATCCTGC-3’
GAPDH_F	5’- AAGGTGAAGGTCGGAGTCAA-3’
GAPDH_R	5’- AATGAAGGGGTCATTGATGG-3’

Table E8. Primers for bisulfite pyrosequencing and the CpG sites interrogated.

IllunimaID	GeneID	Primer	Sequence (5’->3’)	Chr
Not Available	OCT4	F	AAGTTTATATAGATAGGAGATGGGTATA	6
		R	AAACTCCCCTTCAAAATCTATTTTT	
		NF	GGGGAAAAGTTTTAAAAGATTTA	
		NR[a]	ATTCTATTTACAAAAAAATAACCAA	
		S1	TTTGTAATGAGAAGTTTTATTTAAG	
		S2	GATAAATATTATTTTTTATAGATAG	
Not Available	NANOG	F	GGTTGGTTTTAAATTTTTGATTTTAG	12
		R	ACCAATCTCACCAAAACCATTATAA	
		NF	TTAATTTATTGGGATTATAGGGGTG	
		NR[a]	AACAACAAAACCTAAAAACAAACC	
		S1	TTAATTTATTGGGATTATAGGGGTG	
		S2	GAATTATATTTTTGATTTAAAAGTTG	
cg01847719	CAT	F	GGTTTGAAGGATGTTGATAAT	11
		R	ACTCCTTCCAATACTACATCTAATC	
		NF	TATTGGGTTTTTAATTTTGGTTTGT	
		NR[a]	ACTCCTTCCAATACTACATCTAATC	
		S	GAGGTTTTTTGTAGTGTTTTGTATAG	
cg05765254	RPTN	F	TGTGTTTAGGATTTTATAAGGGAATTATAA	1
		R	ATTCTTTACTTTCTTCTCTACCCACCTA	
		NF	TGAATTTTAGGGATAGGATATGTTAAGT	
		NR[a]	TCCTTTCAAAAACAACATAAAACTC	
		S	TGTGGAGTTTTTATGGTTGGGTTTG	
cg04993112	SPRR2A	F	GTAATTTGTTAATGTGTTAGGAGGA	1
		R	AAAATCTAAAATTTTATAAAAAAAA	
		NF	AAGGGGAGATTTAATAAAGGTTTGA	
		NR[a]	AACAAAATCATCAAATAACACAATAC	
		S	ATTTATTTTTGAGTTTGTAGGTATTG	
cg00368577	KRT5	F	GGGGATTTTATGTAATTTTTTAAAAA	12
		R	TTCCATTACCTTAACCCTAAAAAAAA	
		NF	AAATTTTGAGATTTATGGGTTATAG	
		NR[a]	CTAATAAAATTAAAAACTCCTACAAATATA	
		S1	AAATTTTGAGATTTATGGGTTATAG	
		S2	GTTTTATTTTATTAGGGAAGAAATGAG	
cg11752250	ARG2	F	TTGTTTTTTAAAATAGTTTGTATATATTGT	14
		R	ATCTCCTCCAAAAAAAACTAAAACC	
		NF	TTTTTTAAAAGAATTATTTTATATTGAAGA	
		NR[a]	AATCTCTTAAAACAAAACCTACAAAC	
		S1	TTTTTTAAAAGAATTATTTTATATTGAAGA	
		S2	TGGAGATATTTTTGTAGTTTATTTG	
cg16643473	ANO3	F	GGTTGTATTTTGTTTGTGTAATAGAG	11
		R	CAACACATATCAAAAATTCCTACTA	
		NF	AATTTTTTAGTTTTTATAGGTTGAT	
		NR[a]	ACCAAATAACTTTACCAAAATCTTTATC	
		S	AATTTTTTAGTTTTTATAGGTTGAT	

[a]5’ biotinylated; [b]Chromosomal coordinates are based on the UCSC Genome Browser Human February 2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Color Key and Histogram
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0 2 4 6 8
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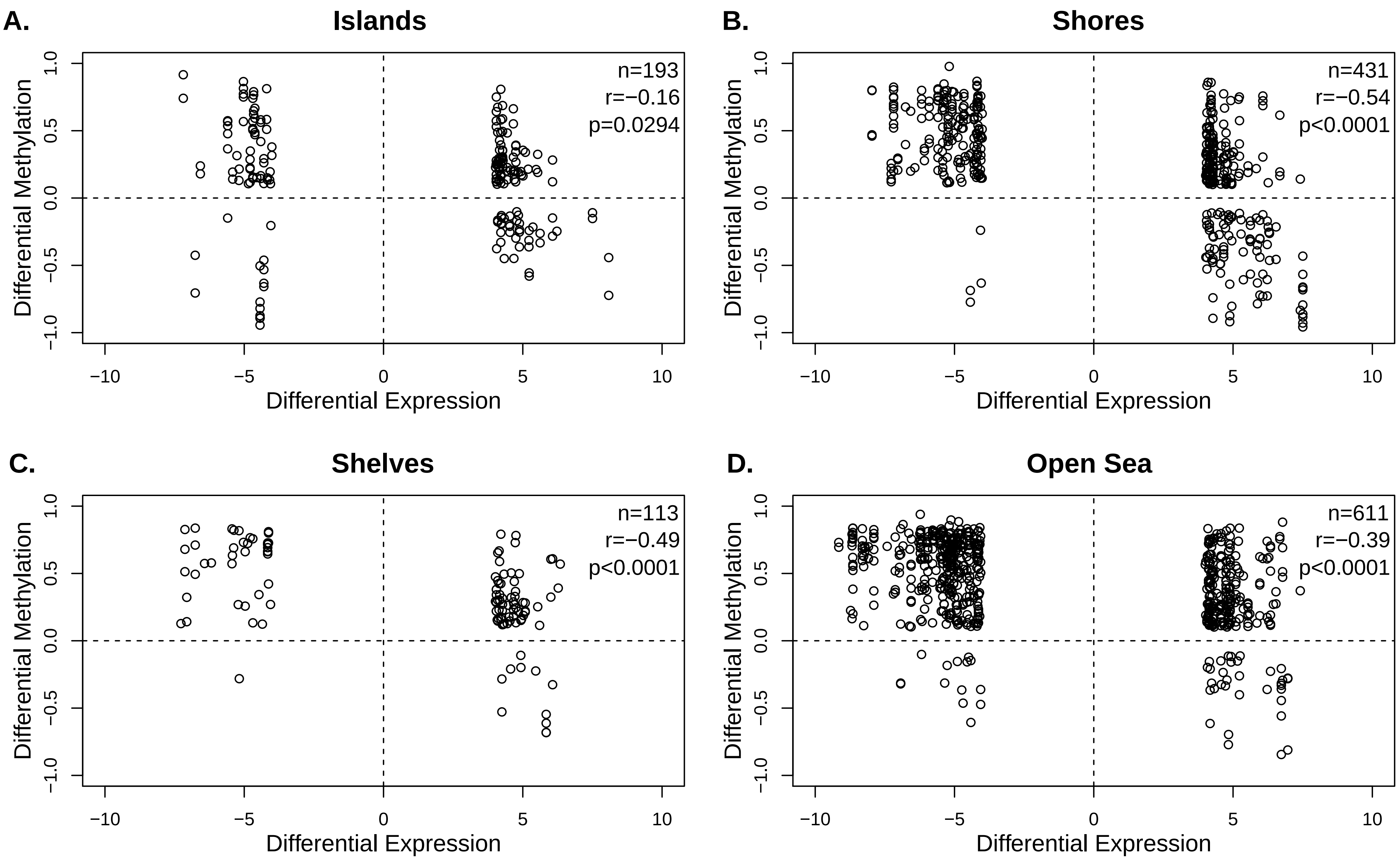
ZNF208
ZNF729
CTSF
ZNF98
RP11–313J2.1
ZNF560
FAAH
CUZD1
TRPC4
RP11–455F5.3
NUDT14
FTH1P3
AASS
NEC_iPSC_4
NEC_iPSC_3
NEC_iPSC_1
NEC_iPSC_2
ESC_2
ESC_1
cNE_1
cNE_2
cNE_3
NE_1
NE_3
NE_2
B.
CTSF
Normalzed Expression (GADPH)
4
3
2
1
0
-1
*
n.s.
***
NE
cNE
ESC
NEC-iPSC
HFF-iPSC
PBMC-iPSC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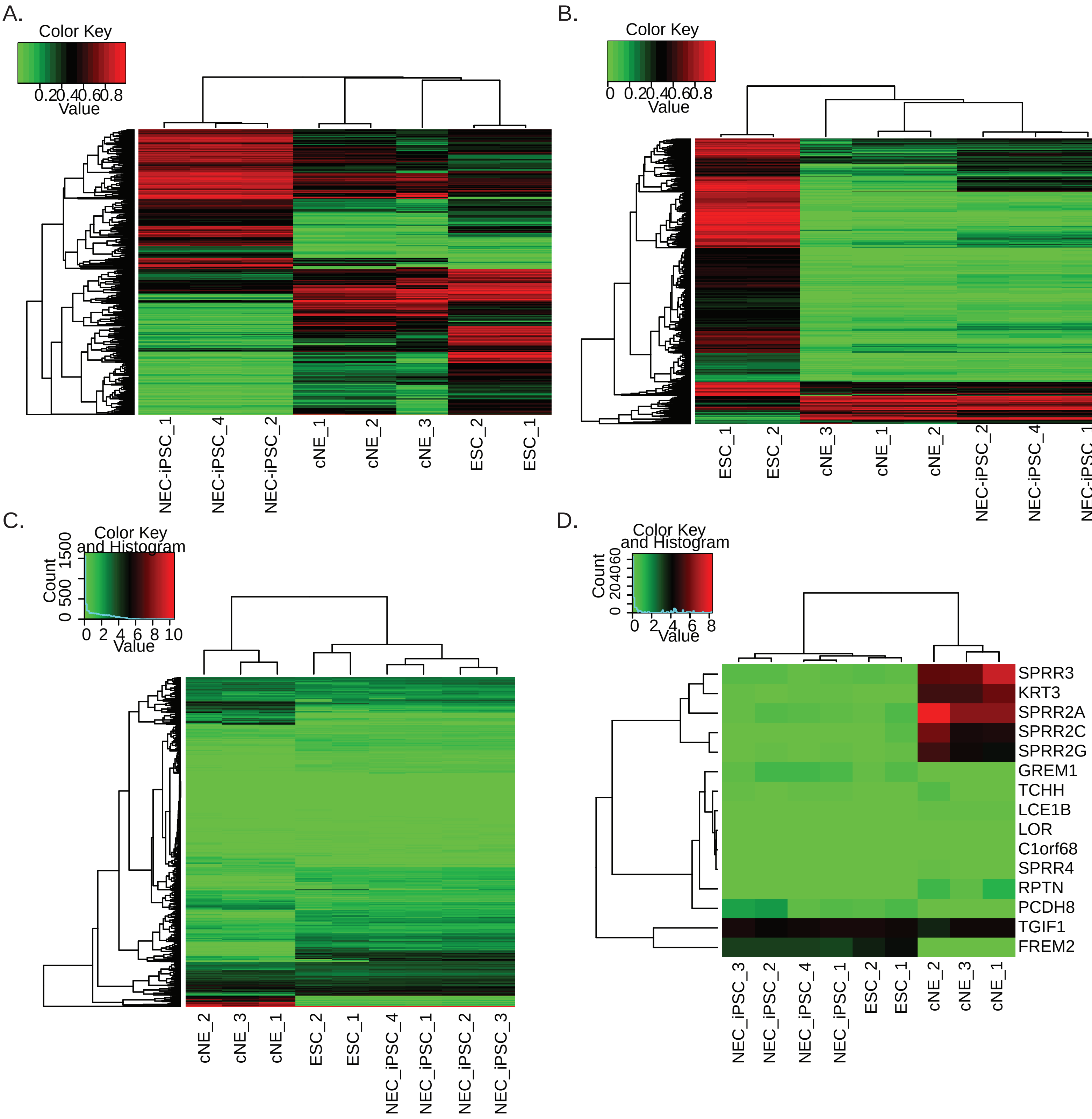
p=0.0294
B.
Shores
n=431
r=−0.54
p<0.0001
C.
Shelves
n=113
r=−0.49
p<0.0001
D.
Open Sea
n=611
r=−0.39
p<0.0001
Differential Methylation
1.0
0.5
0.0
−0.5
−1.0
Differential Expression
−10
−5
0
5
10


A.
Color Key
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Value
NEC-iPSC_1
NEC-iPSC_4
NEC-iPSC_2
cNE_1
cNE_2
cNE_3
ESC_2
ESC_1
B.
Color Key
0 0.2 0.4 0.6 0.8
Value
ESC_1
ESC_2
cNE_3
cNE_1
cNE_2
NEC-iPSC_2
NEC-iPSC_4
NEC-iPSC_1
C.
Color Key
and Histogram
Count
0 500 1500
0 2 4 6 8 10
Value
cNE_2
cNE_3
cNE_1
ESC_2
ESC_1
NEC_iPSC_4
NEC_iPSC_1
NEC_iPSC_2
NEC_iPSC_3
D.
Color Key
and Histogram
Count
0 20 40 60
0 2 4 6 8
Value
SPRR3
KRT3
SPRR2A
SPRR2C
SPRR2G
GREM1
TCHH
LCE1B
LOR
C1orf68
SPRR4
RPTN
PCDH8
TGIF1
FREM2
NEC_iPSC_3
NEC_iPSC_2
NEC_iPSC_4
NEC_iPSC_1
ESC_2
ESC_1
cNE_2
cNE_3
cNE_1