

Supporting Information

Chromosomal repositioning and gene regulation of cells on a micropillar array

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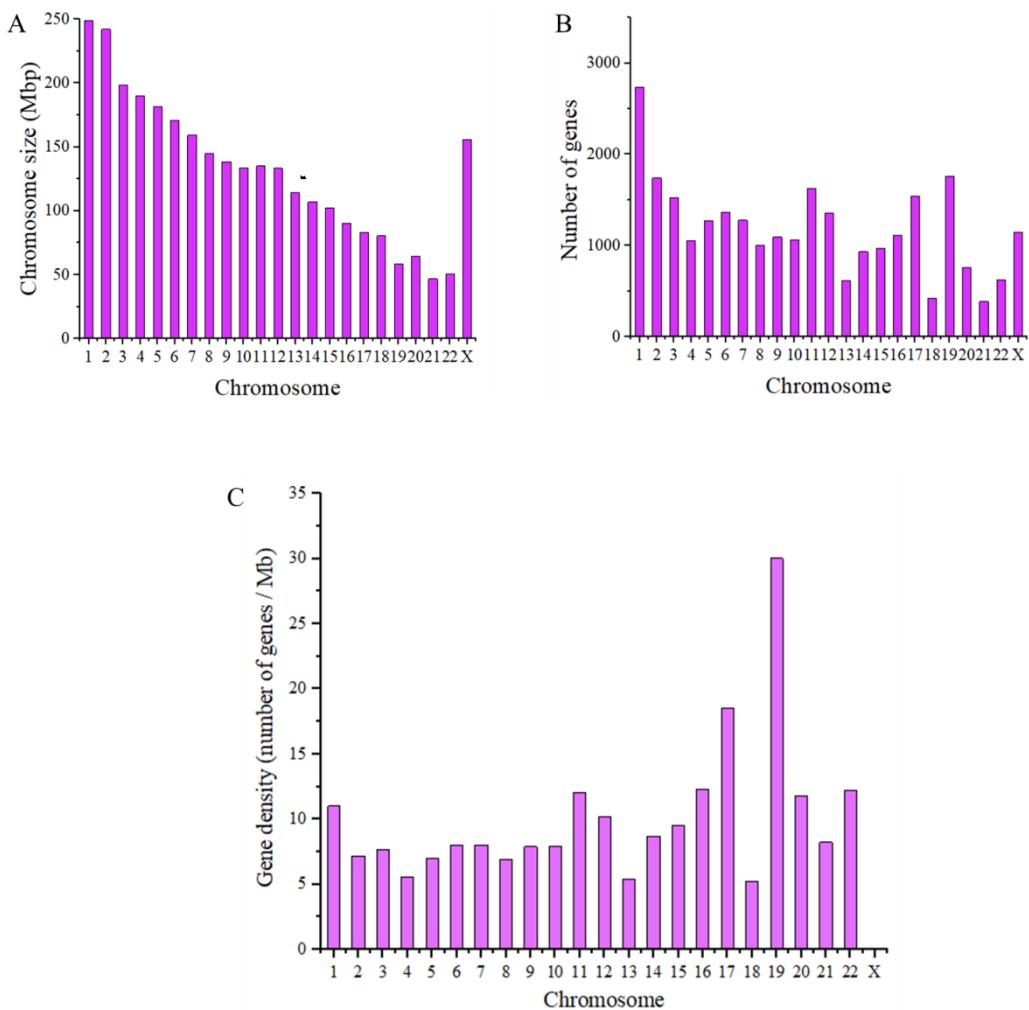


Figure S1. Human chromosomal sizes, number of genes on each chromosome, and gene densities of the human chromosomes. Drawn by the authors based on the data released in Atlas of Genetics and Cytogenetics in Oncology and Haematology (URL <http://AtlasGeneticsOncology.org> on 25th June, 2020) with permission [S1]. Since HeLa cells (female) were employed as the model cell type, the Y chromosome is not shown in this figure.

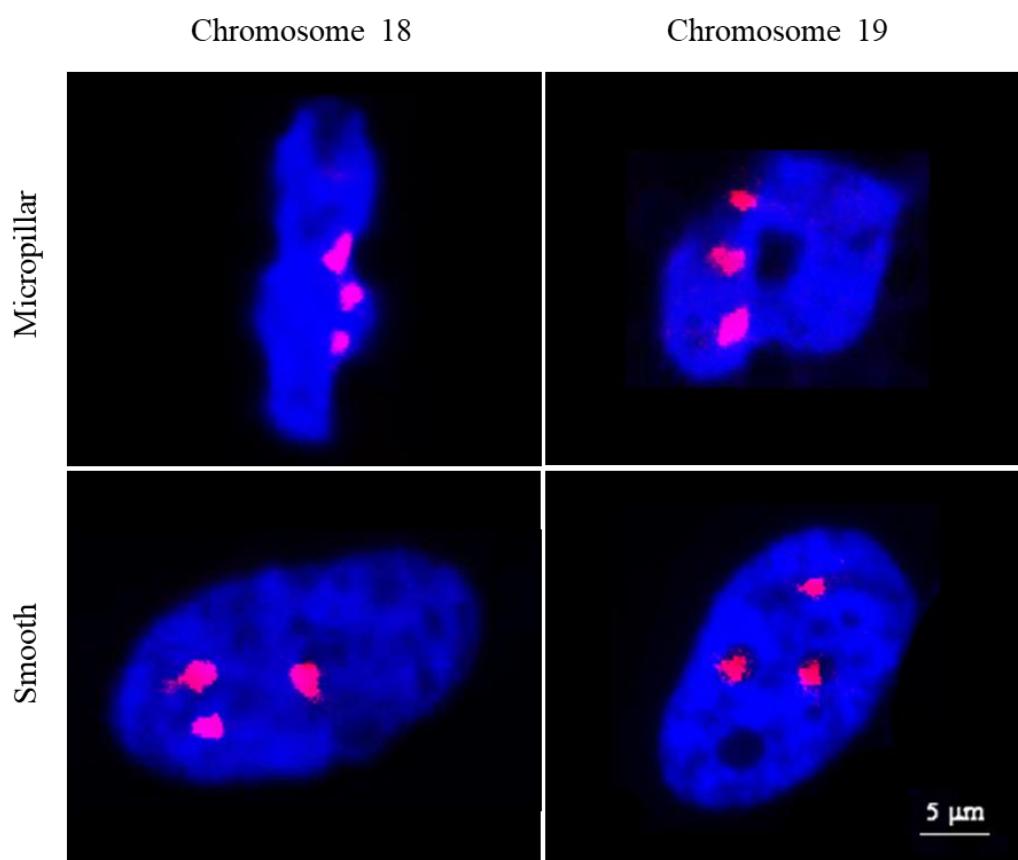


Figure S2. Fluorescence micrographs of FISH staining for chromosomal territory of the aneuploids of chromosomes 18 and 19 of HeLa cells on the micropillar array and smooth PLGA surface.

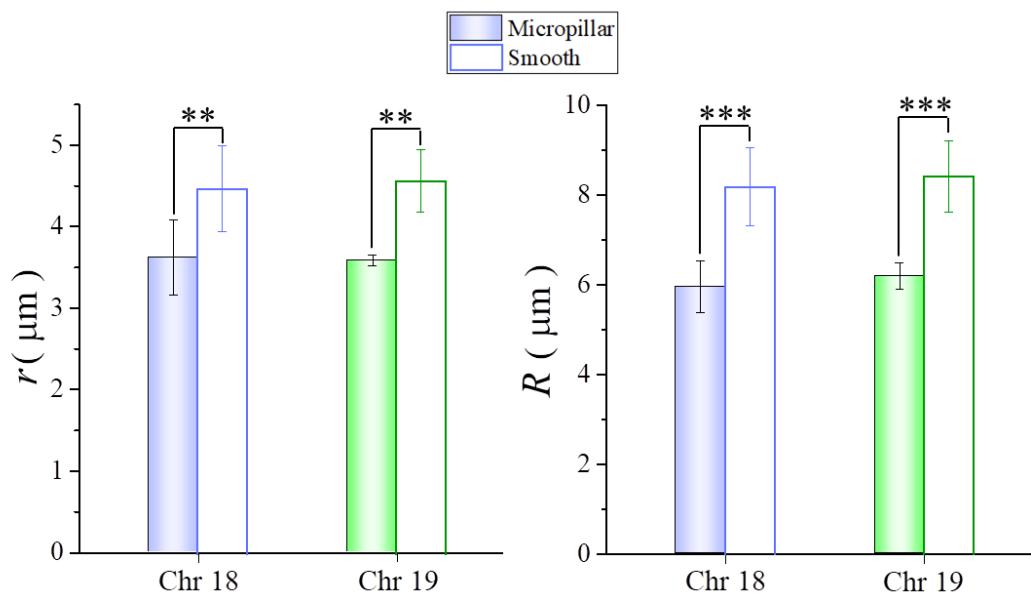


Figure S3. Distribution of chromosomes 18 and 19 in the nuclei of HeLa cells on the micropillared and smooth surfaces. r , the distance from the centroid of a nucleus to the centroid of a chromosome in two-dimensional projection; R , the distance from the centroid of the nucleus to the edge of the nucleus passing through the centroid of the chromosome in two-dimensional projection. ‘**’: $p < 0.01$; ‘***’: $p < 0.001$.

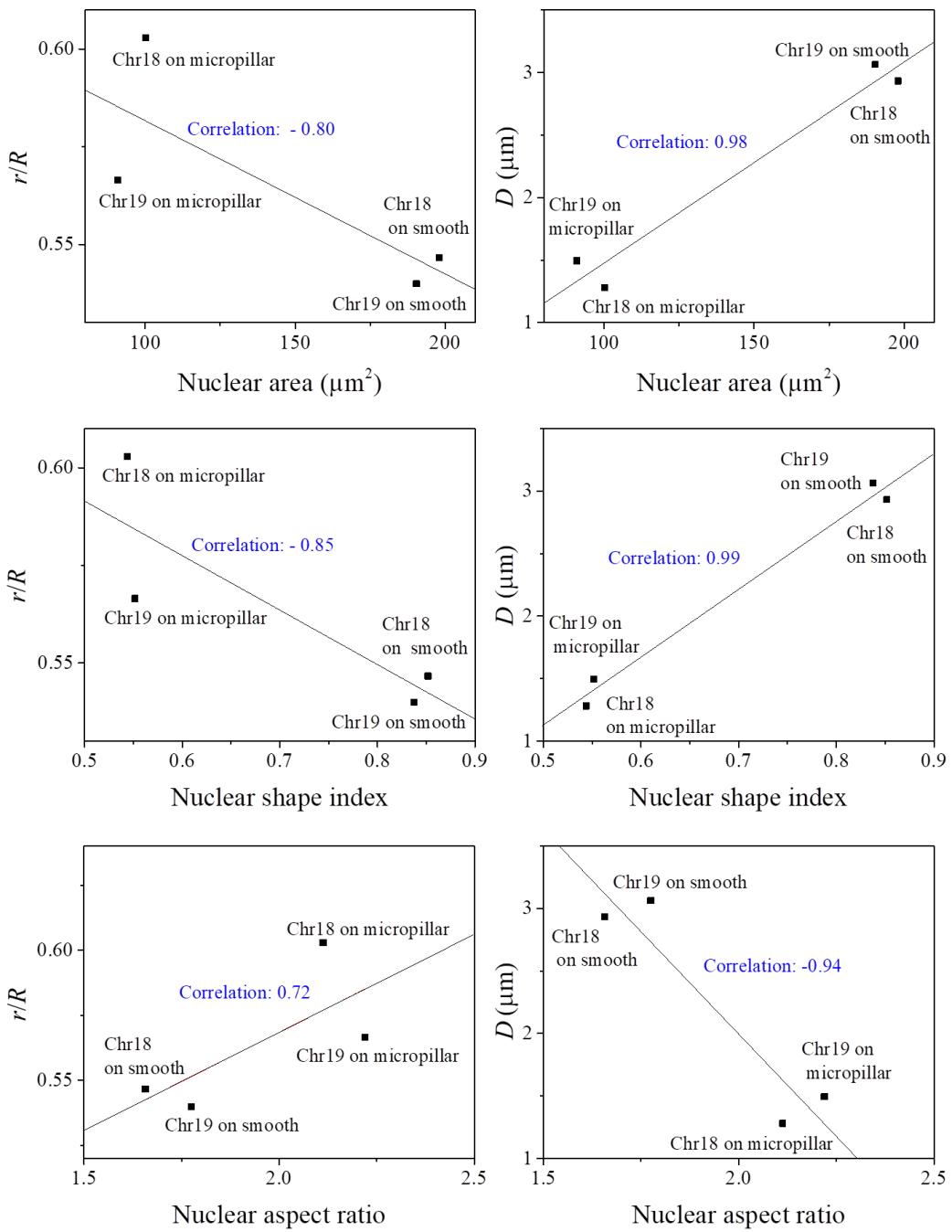


Figure S4. Relations of chromosomal positioning to nuclear area, nuclear shape index and nuclear aspect ratio of HeLa cells. “Correlation” means the linear correlation coefficient.

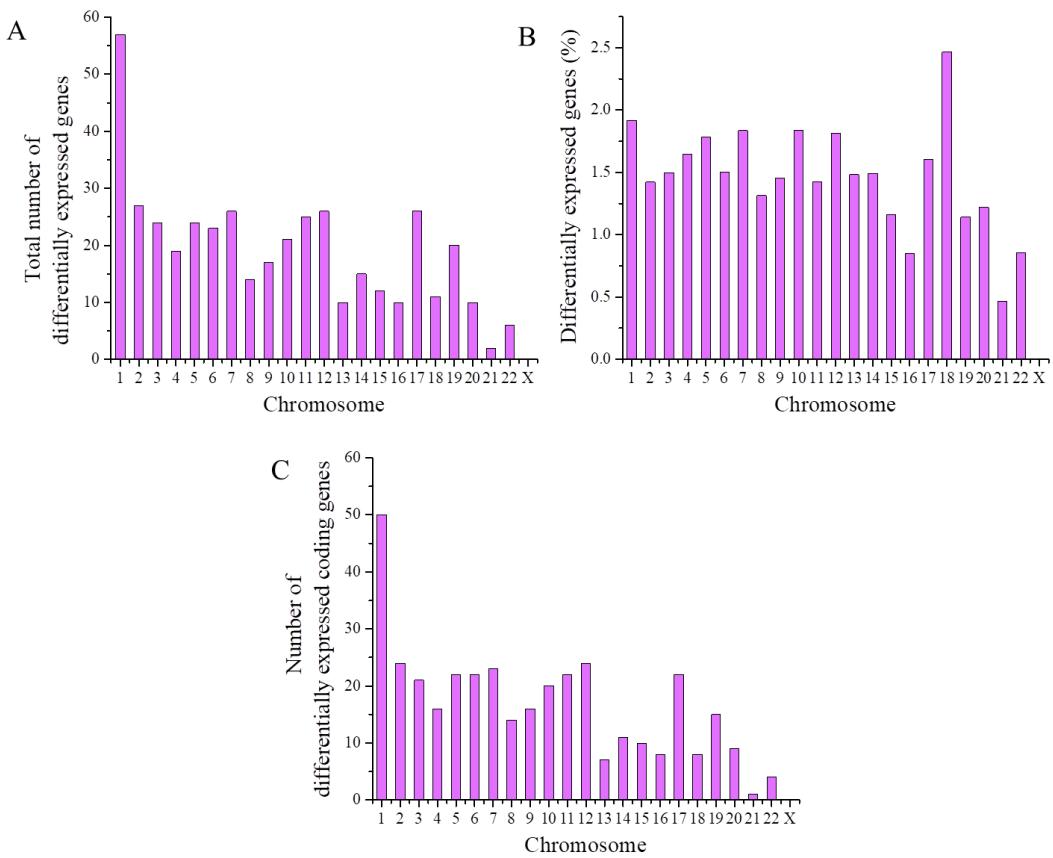


Figure S5. Number and fraction of differentially expressed genes on each chromosome. (A) Total number of the differentially expressed genes; (B) Fraction of differentially expressed genes; (C) Number of differentially expressed coding genes. Fraction of differentially expressed genes (%) = Number of differentially expressed genes on a chromosome / number of total genes on the chromosome × 100%.

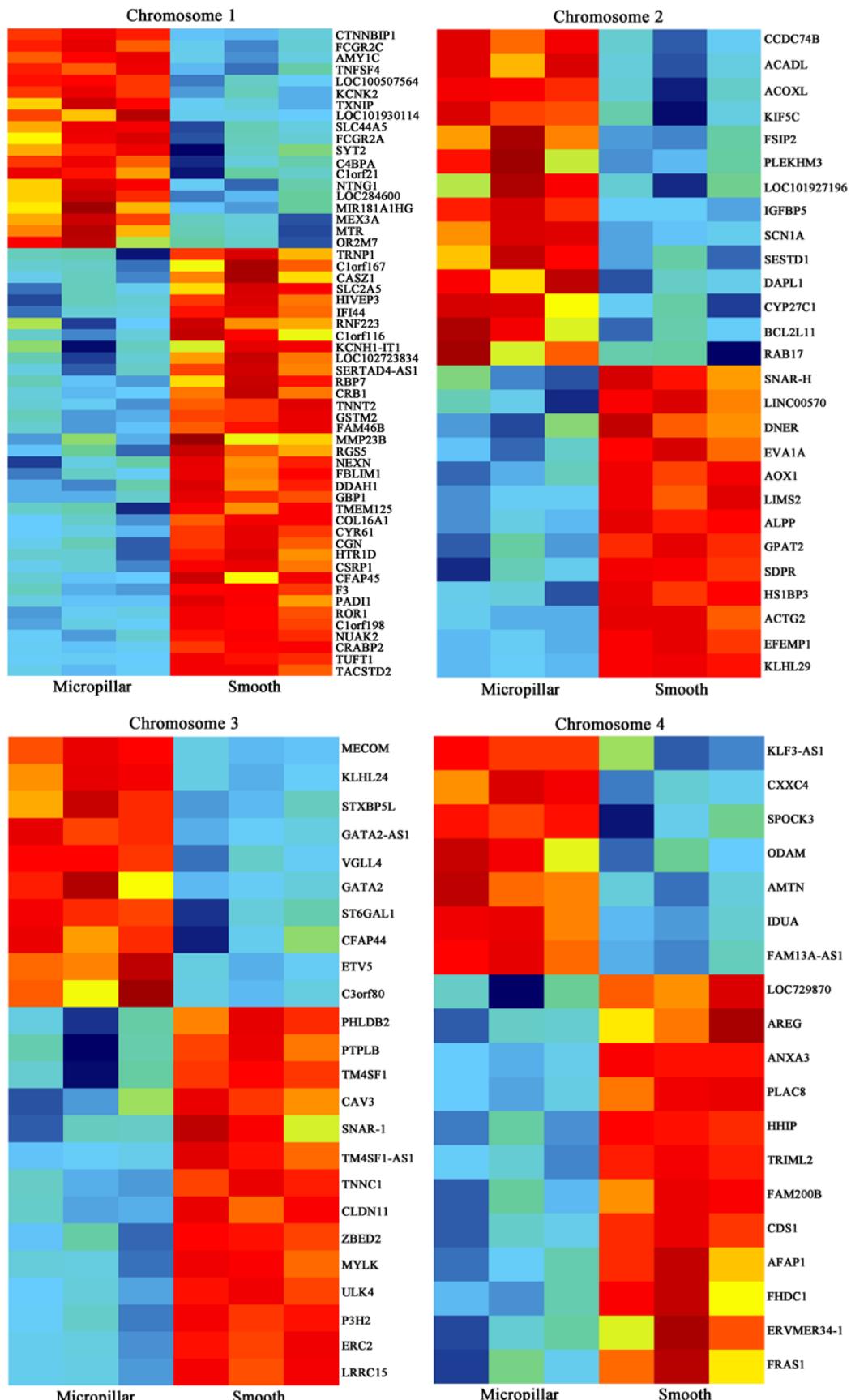


Figure S6-1. Heatmaps of differentially expressed genes on chromosomes 1, 2, 3, 4 of HeLa cells on the micropillar array.

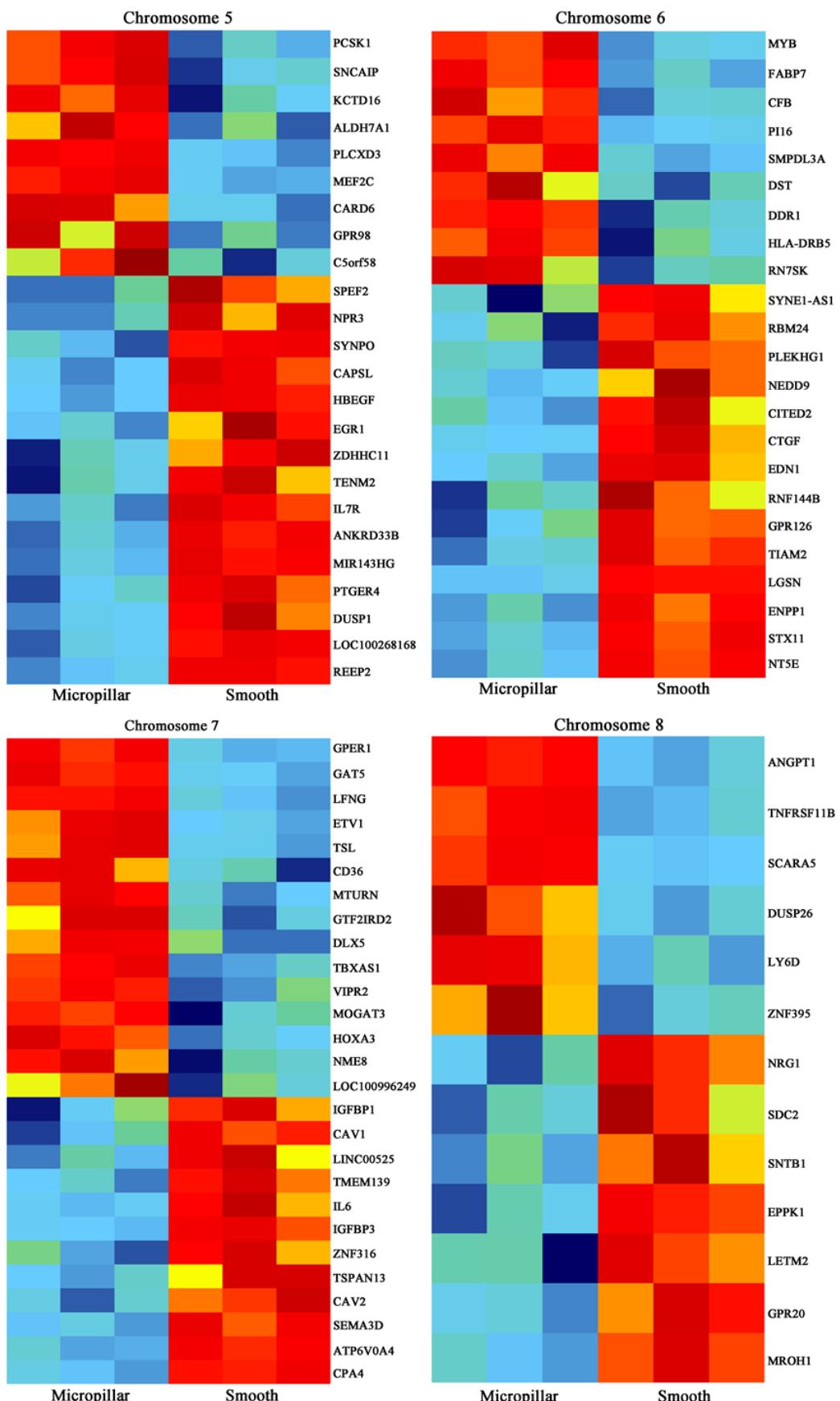


Figure S6-2. Heatmaps of differentially expressed genes on chromosomes 5, 6, 7, 8 of HeLa cells on the micropillar array.

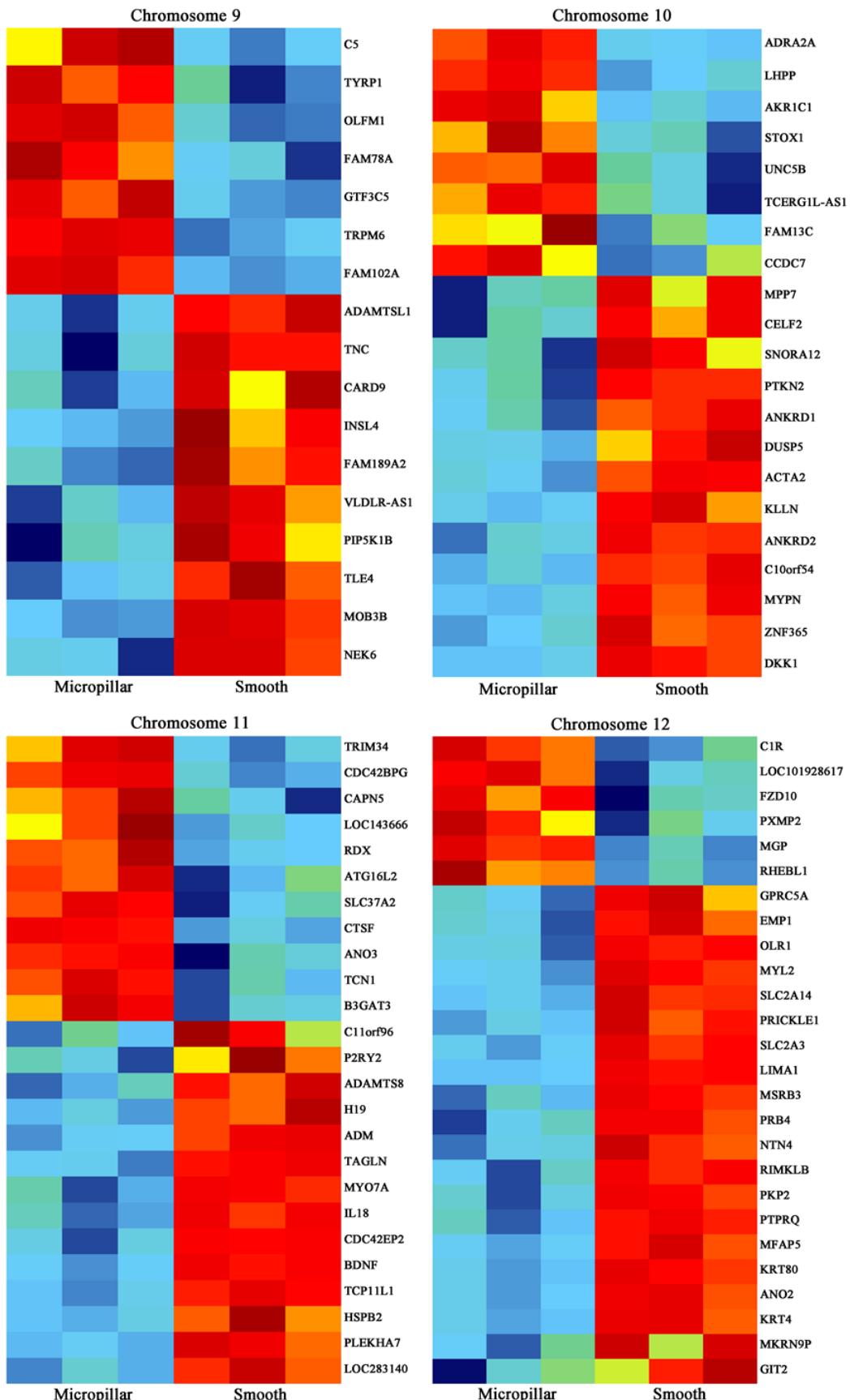


Figure S6-3. Heatmaps of differentially expressed genes on chromosomes 9, 10, 11, 12 of HeLa cells on the micropillar array.

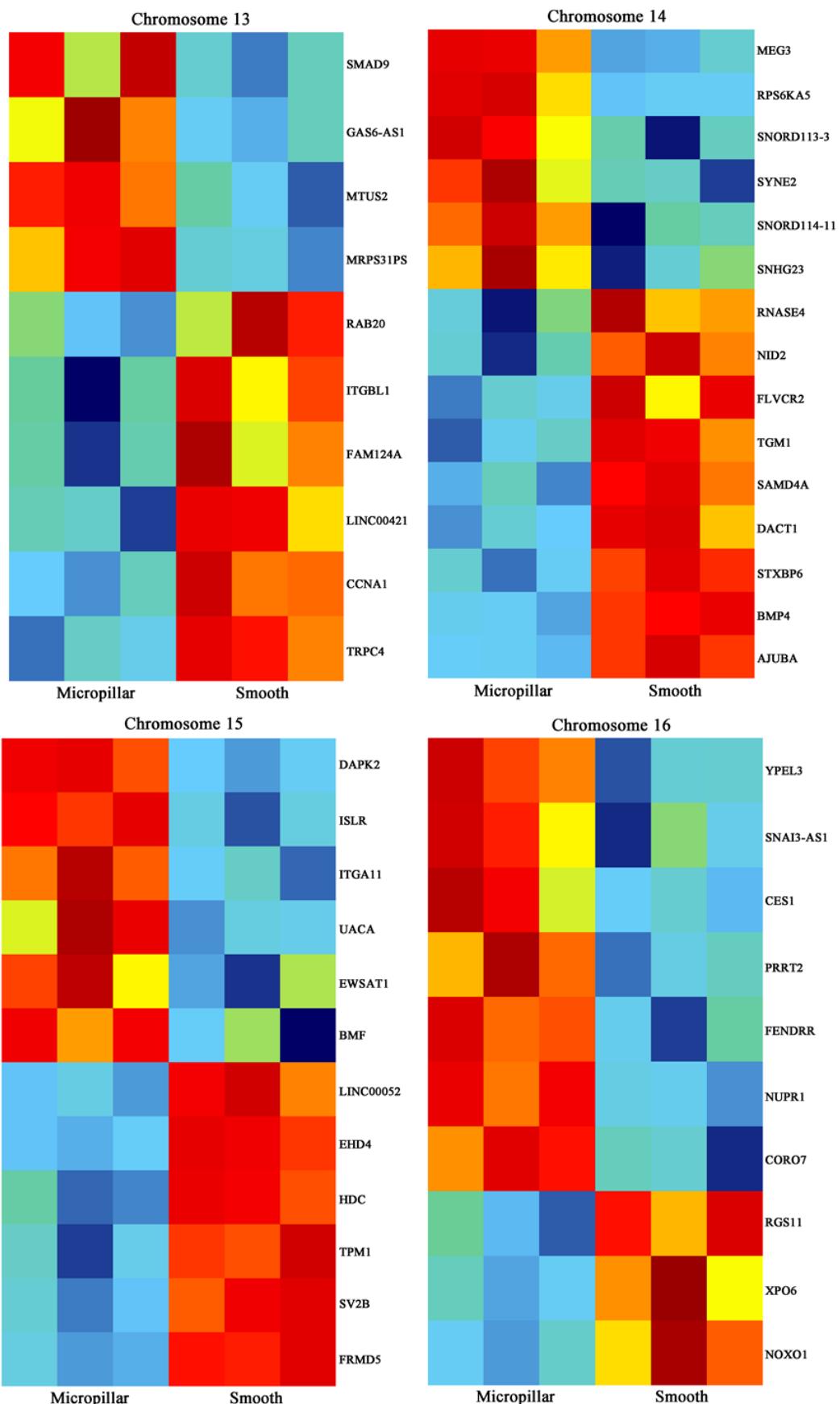


Figure S6-4. Heatmaps of differentially expressed genes on chromosomes 13, 14, 15, 16 of HeLa cells on the micropillar array.

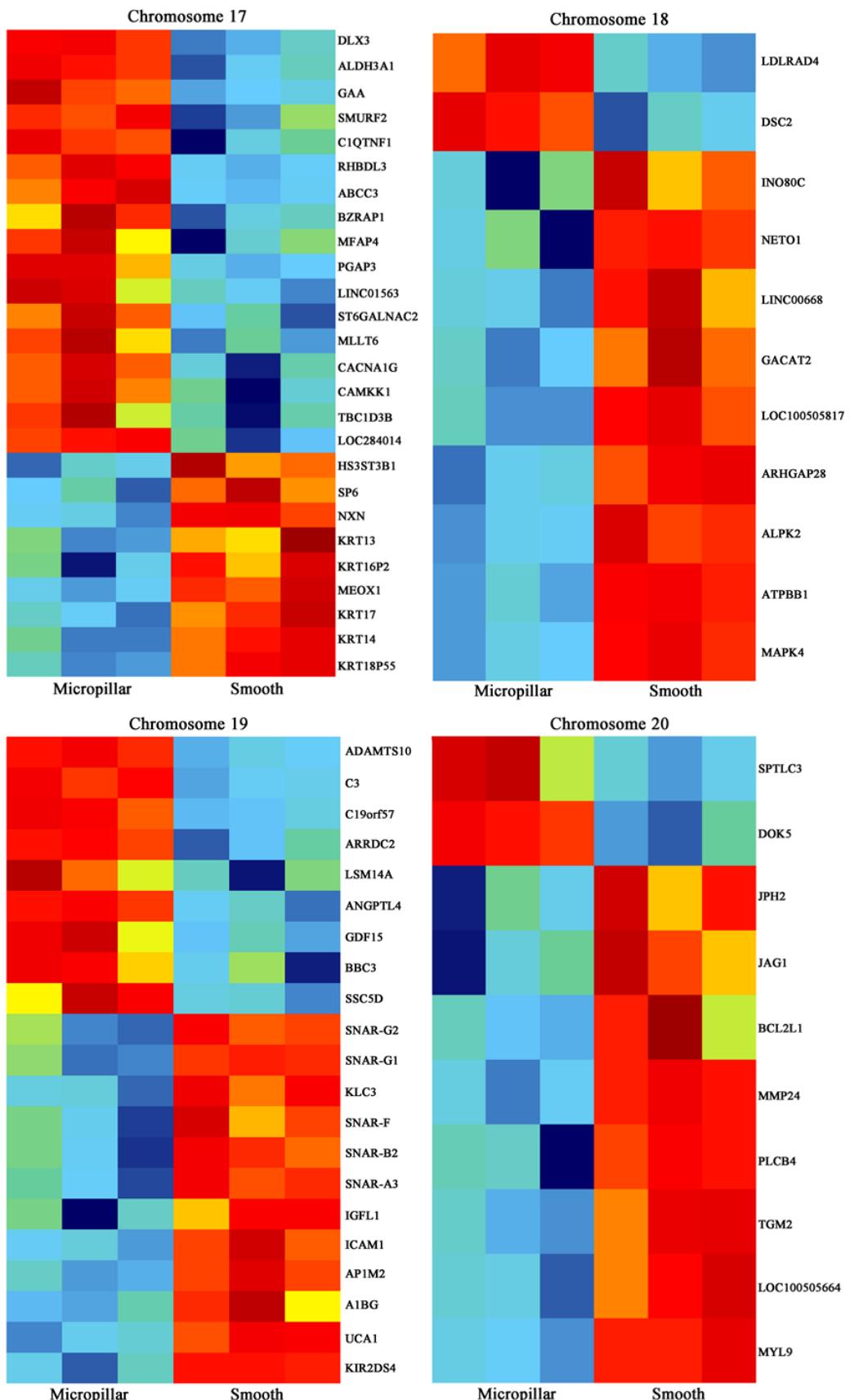


Figure S6-5. Heatmaps of differentially expressed genes on chromosomes 17, 18, 19, 20 of HeLa cells on the micropillar array.

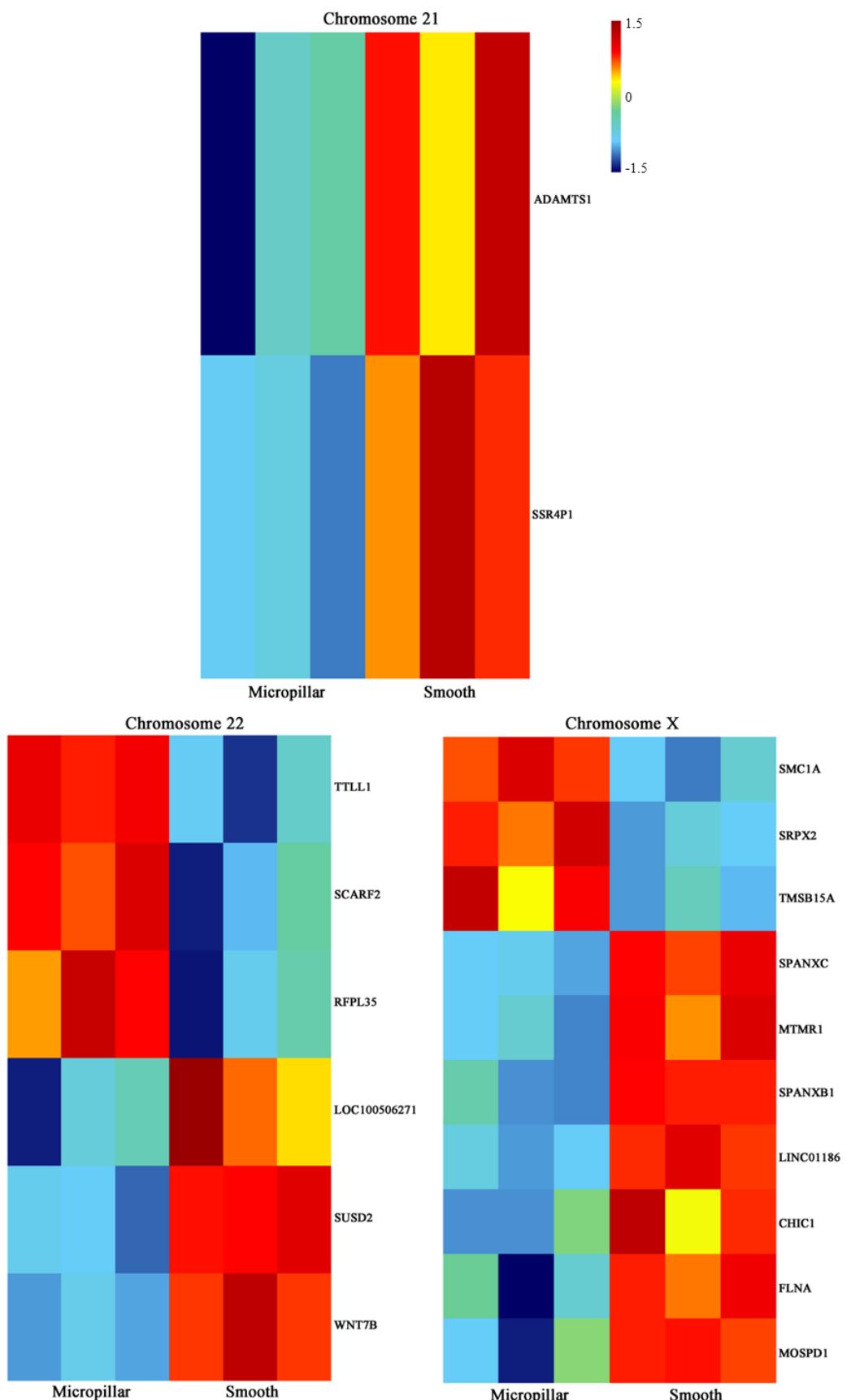


Figure S6-6. Heatmaps of differentially expressed genes on chromosomes 21, 22, X of HeLa cells on the micropillar array. Red, high expression; Blue, low expression.

The numbers 1.5, 0 -1.5 in the ruler reflect the maximum, medium, and minimum values of gene signals of the differentially expressed genes. The rows reflect the samples, and every line reflects one gene. Three rows on the left reflect the differentially expressed genes of HeLa cells on micropillar array; the other three rows on the right reflect the differentially expressed genes of HeLa cells on the smooth surface.

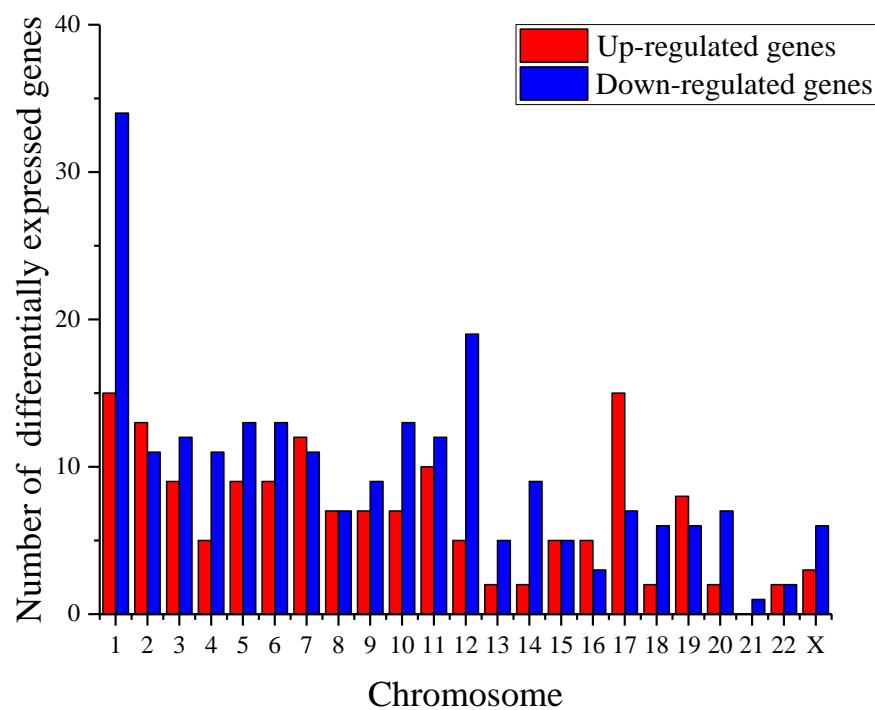


Figure S7. Numbers of up- and down-regulated protein-coding genes of the chromosomes.

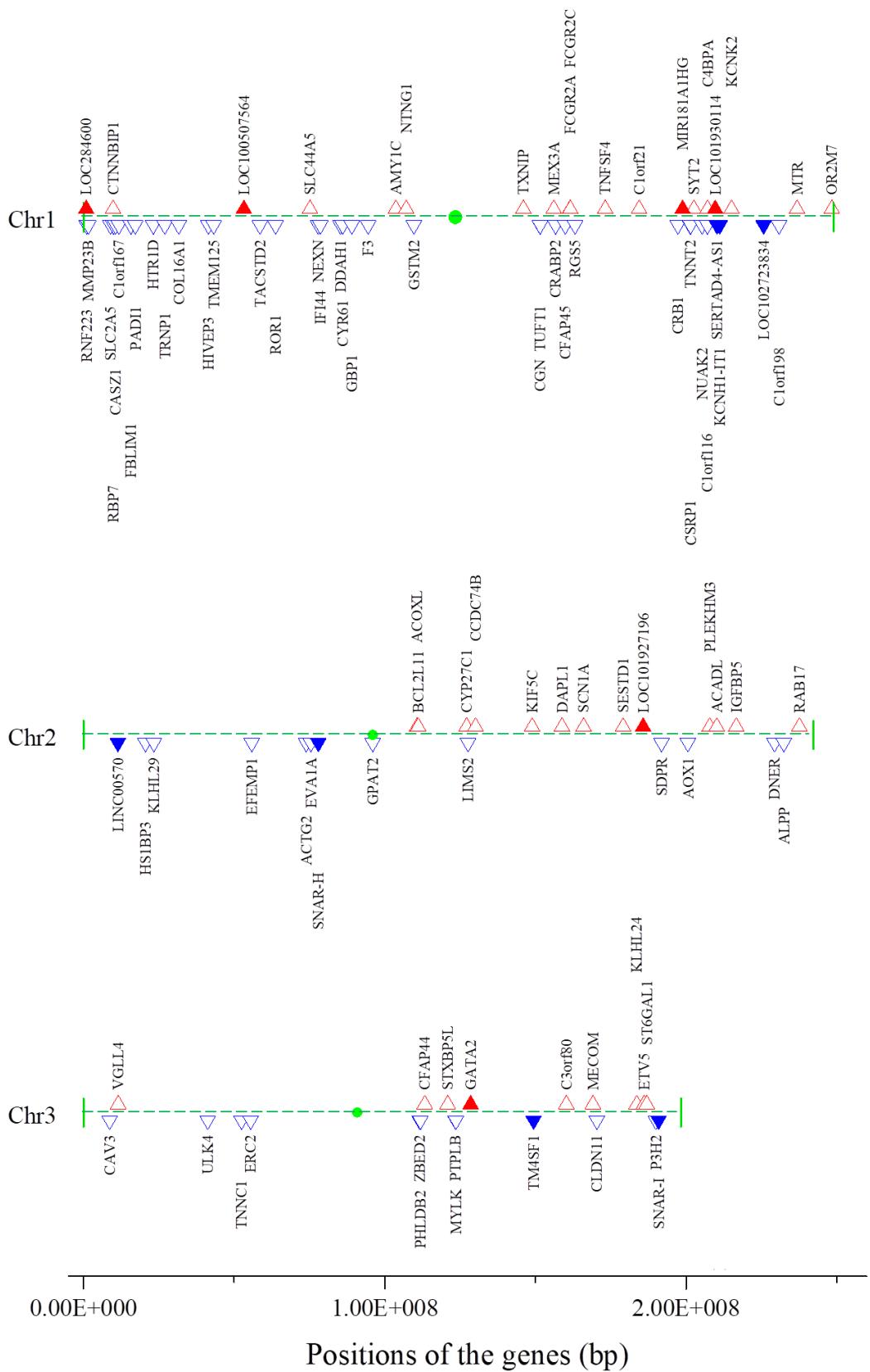


Figure S8-1. Cytogenetic mapping of up and down regulated genes on chromosomes 1, 2 and 3.

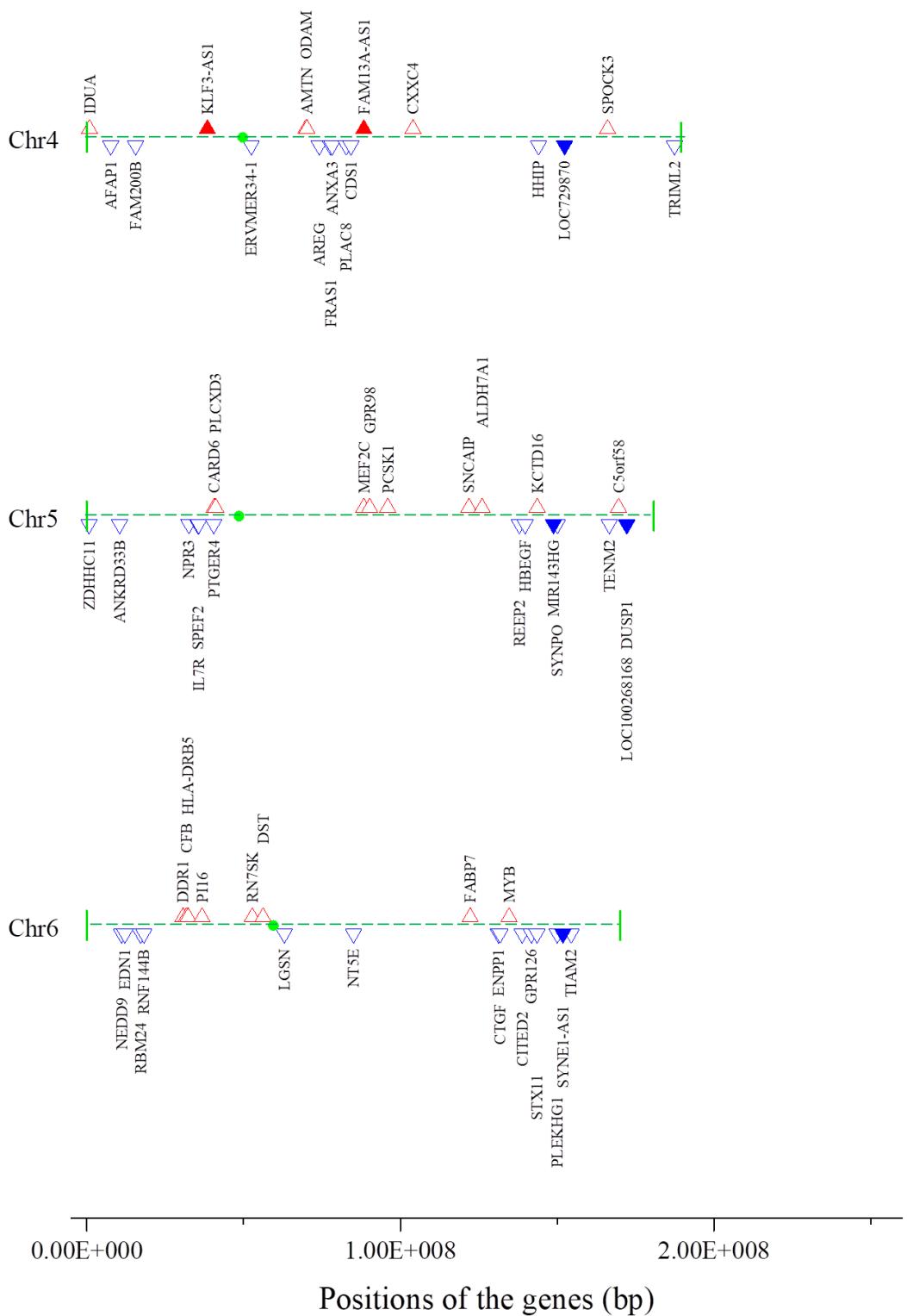


Figure S8-2. Cytogenetic mapping of up and down regulated genes on chromosomes 4, 5, 6.

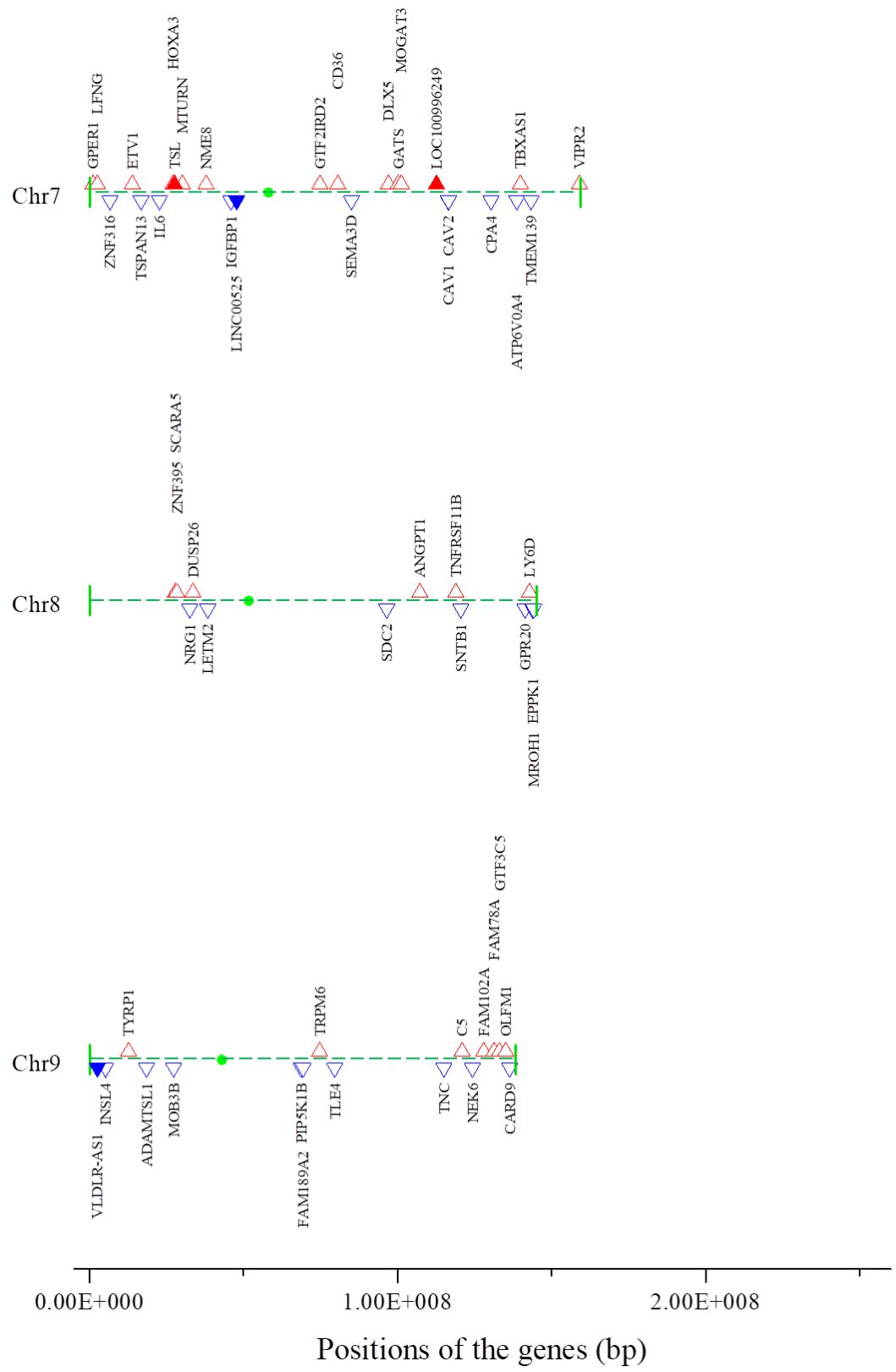


Figure S8-3. Cytogenetic mapping of up and down regulated genes on chromosomes 7, 8, 9.

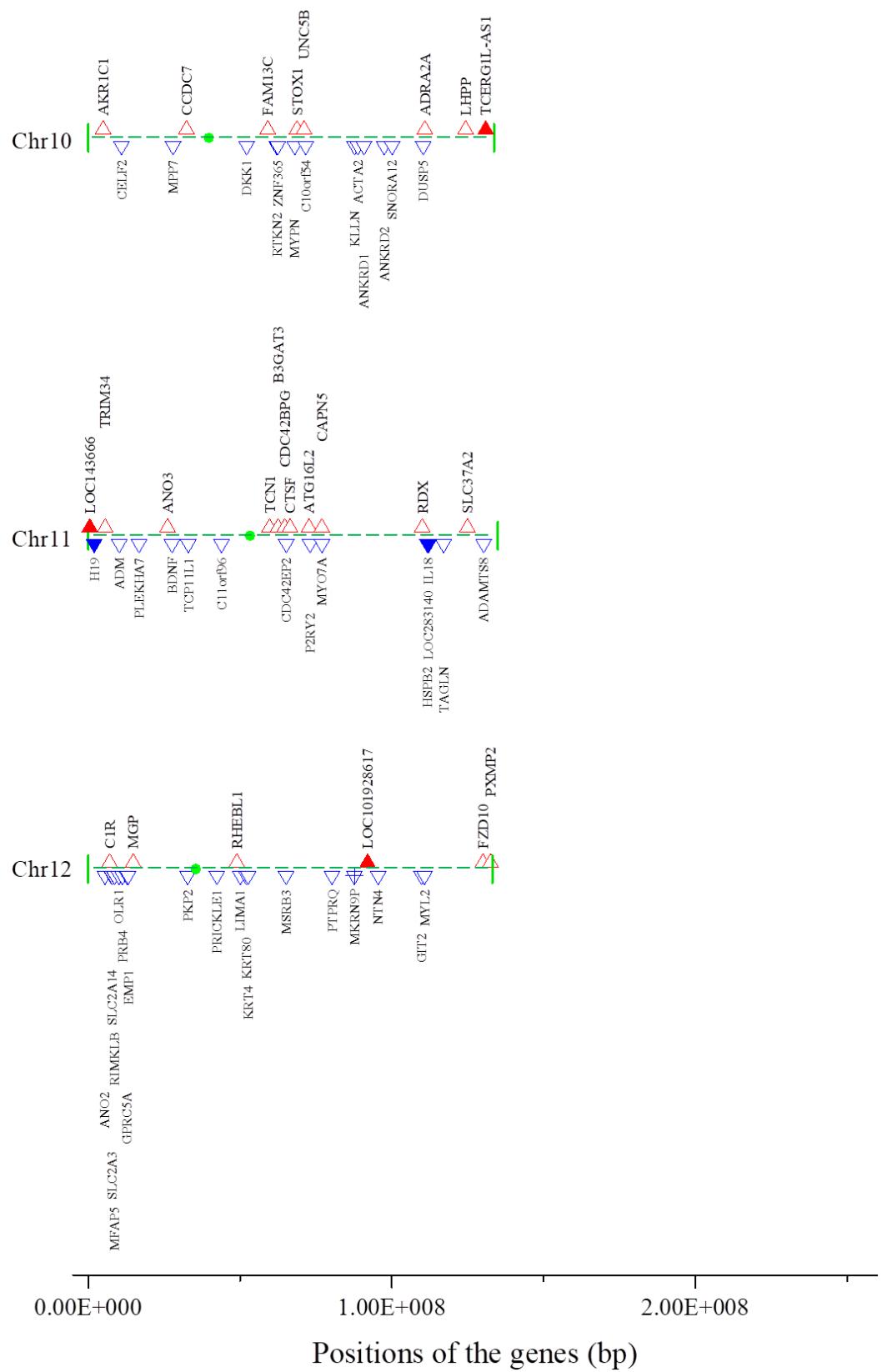


Figure S8-4. Cytogenetic mapping of up and down regulated genes on chromosomes 10, 11, 12

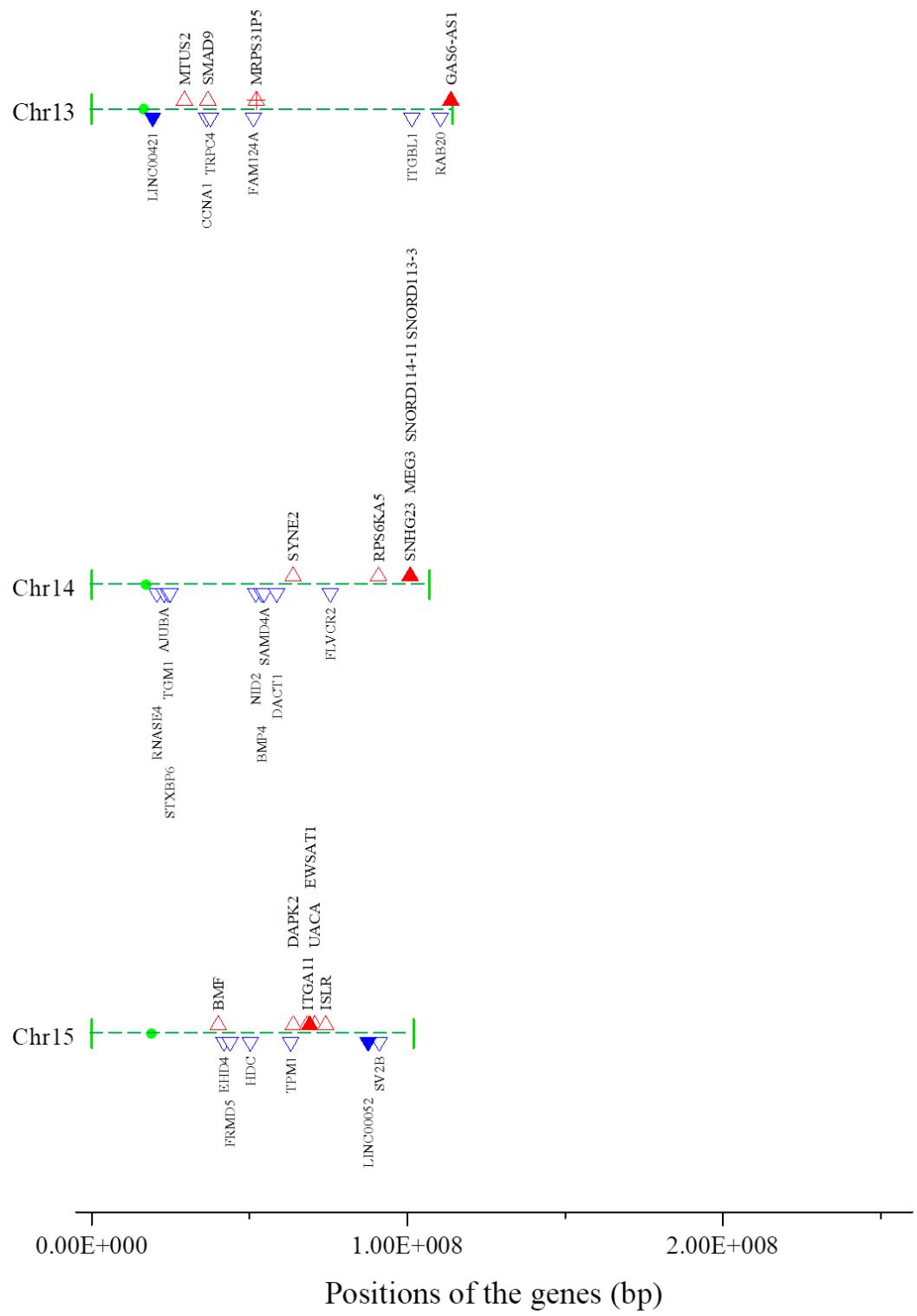


Figure S8-5. Cytogenetic mapping of up and down regulated genes on chromosomes 13, 14, 15

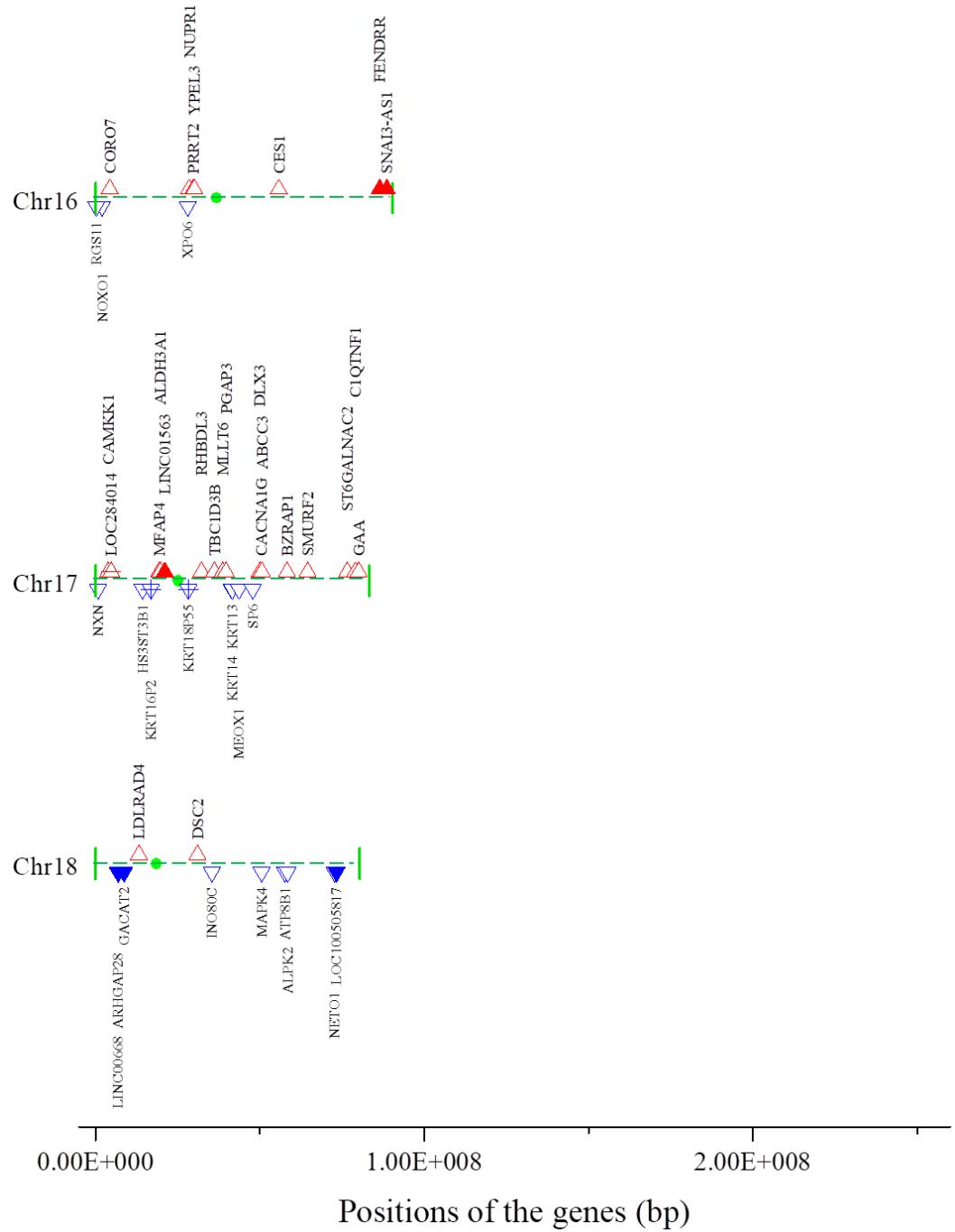


Figure S8-6. Cytogenetic mapping of up and down regulated genes on chromosomes 16, 17, 18

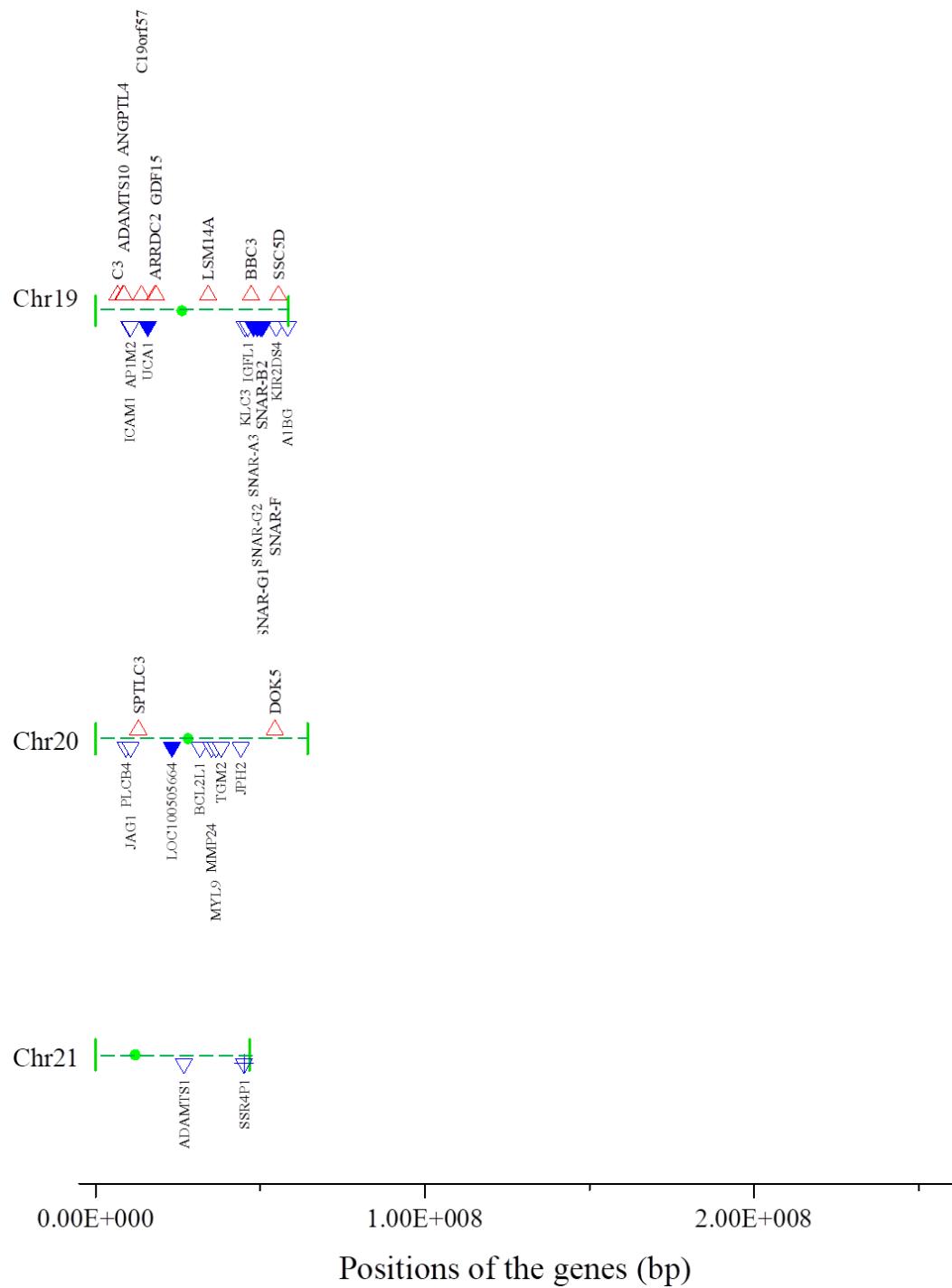


Figure S8-7. Cytogenetic mapping of up and down regulated genes on chromosomes 19, 20, 21

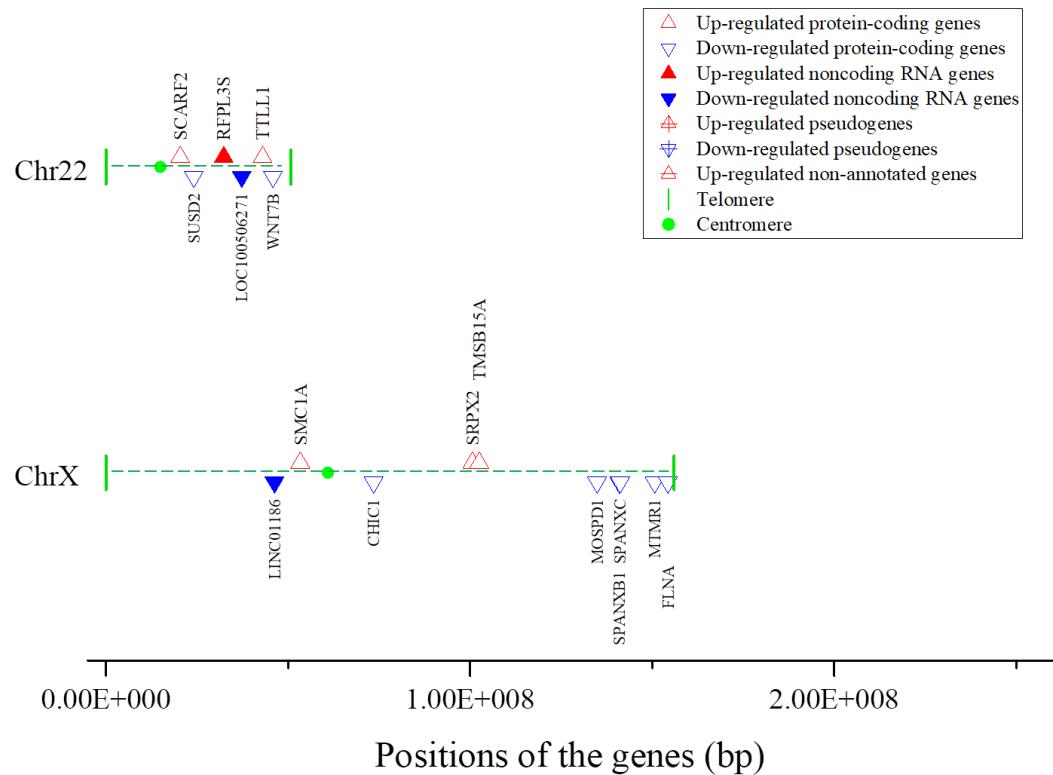
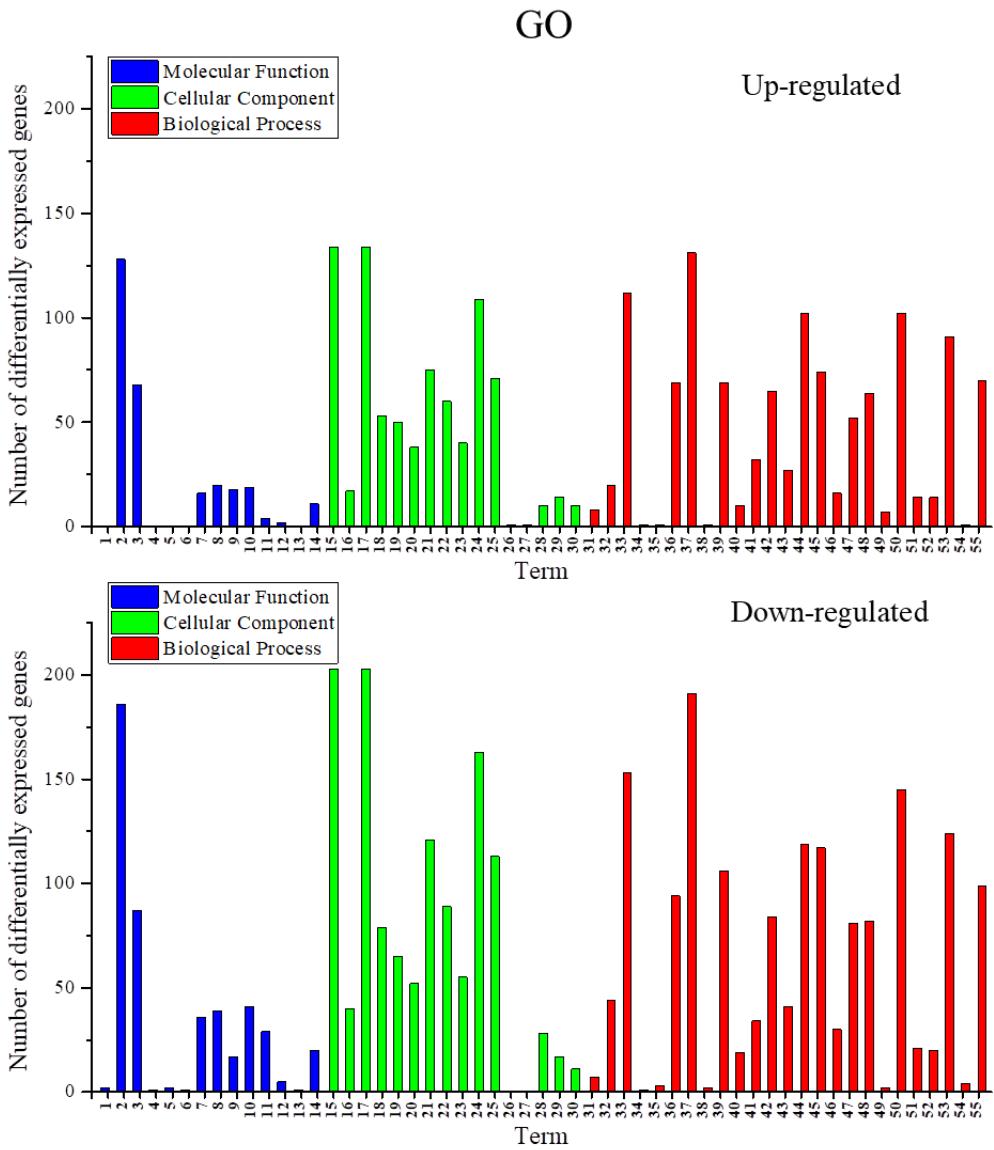


Figure S8-8. Cytogenetic mapping of up and down regulated genes on chromosomes 22 and X



1 Antioxidant activity, 2 Binding, 3 Catalytic activity, 4 Chemoattractant activity, 5 Chemorepellent activity, 6 Electron carrier activity, 7 Molecular function regulator, 8 Molecular transducer activity, 9 Nucleic acid binding transcription factor activity, 10 Signal transducer activity, 11 Structural molecule activity, 12 Transcription factor activity, protein binding, 13 Translation regulator activity, 14 Transporter activity, 15 Cell, 16 Cell junction, 17 Cell part, , 18 Extracellular region, 19 Extracellular region part, 20 Macromolecular complex, 21 Membrane, 22 Membrane part, 23 Membrane-enclosed lumen, 24 Organelle, 25 Organelle part, 26 Other organism, 27 Other organism part, 28 Supramolecular complex, 29 Synapse, 30 Synapse part, 31 Behavior, 32 Biological adhesion, 33 Biological regulation, 34 Cell aggregation, 35 Cell killing, 36 Cellular component organization or biogenesis, 37 Cellular process, 38 Detoxification, 39 Developmental process, 40 Growth, 41 Immune system process, 42 Localization, 43 Locomotion, 44 Metabolic process, 45 Multicellular organismal process, 46 Multi-organism process, 47 Negative regulation of biological process, 48 Positive regulation of biological process, 49 Presynaptic process involved in chemical synaptic transmission, 50 Regulation of biological process, 51 Reproduction, 52 Reproductive process, 53 Response to stimulus, 54 Rhythmic process, 55 Signaling

Figure S9. The biological function category of GO (gene ontology) classification of the up- and down-regulated genes of HeLa cells on the micropillar array.

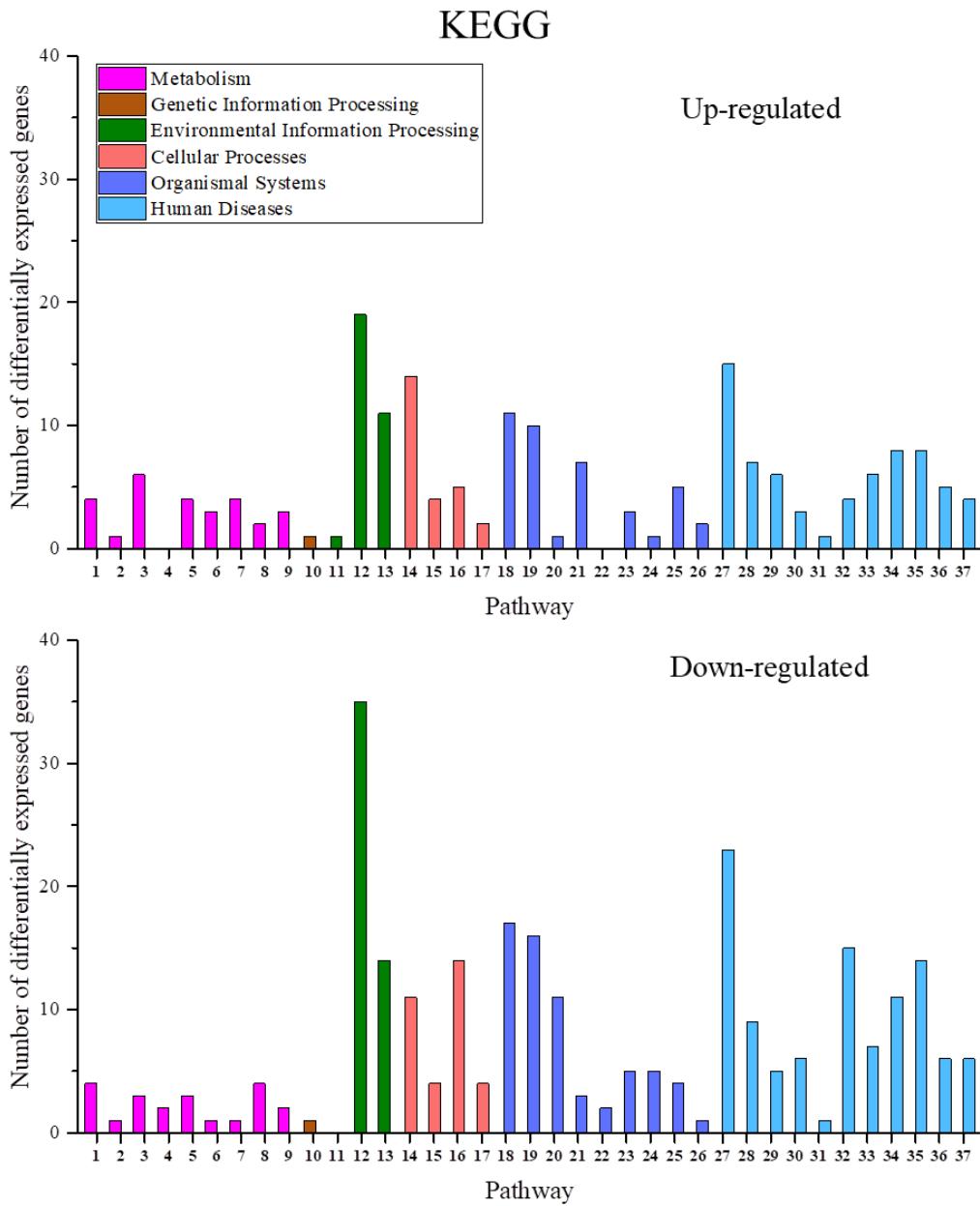
Note:

Gene Ontology Consortium aims to produce a dynamic, controlled vocabulary

which can be applied to all eukaryotes even when knowledge of gene and protein roles in cells is accumulating and changing [S2].

Analysis of Gene Ontology (GO) can reflect three aspects, including molecular function, cellular component, and biological process. The molecular function describes molecular-level activities performed by gene products that occur at the molecular level; the cellular component describes the locations relative to cellular structures in which a gene product performs a function, either cellular compartments (e.g., mitochondrion), or stable macromolecular complexes of which they are parts (e.g., the ribosome); the biological process describes the larger processes or ‘biological programs’ accomplished by multiple molecular activities.

The Binding term describes the selective, non-covalent, often stoichiometric, interaction of a molecule with one or more specific sites on another molecule, including the chemical binding and the protein binding related to the gene product. The Binding term mainly describes the activity of an enzyme or transporter. The Cell term is the basic structural and functional unit of all organisms. The Cell Part term is any constituent part of a cell, the basic structural and functional unit of all organisms. The Cellular Process term describes any process that is carried out at the cellular level, but not necessarily restricted to a single cell.



1 Carbohydrate metabolism, 2 Energy metabolism, 3 Lipid metabolism, 4 Nucleotide metabolism, 5 Amino acid metabolism, 6 Metabolism of other amino acids, 7 Glycan biosynthesis and metabolism, 8 Metabolism of cofactors and vitamins, 9 Xenobiotics biodegradation and metabolism, 10 Folding, sorting and degradation, 11 Membrane transport, 12 Signal transduction, 13 Signaling molecules and interaction, 14 Transport and catabolism, 15 Cell growth and death, 16 Cellular community – eukaryotes, 17 Cell motility, 18 Immune system, 19 Endocrine system, 20 Circulatory system, 21 Digestive system, 22 Excretory system, 23 Nervous system, 24 Sensory system, 25 Development and regeneration, 26 Environmental adaptation, 27 Cancers: overview, , 28 Cancers: specific types, 29 Immune diseases, 30 Neurodegenerative diseases, 31 Substance dependence, 32 Cardiovascular diseases, 33 Endocrine and metabolic diseases, 34 Infectious diseases: bacterial, 35 Infectious diseases: viral, 36 Infectious diseases: parasitic, 37 Drug resistance: antineoplastic

Figure S10. KEGG pathway functional classification and annotation of up- and down-regulated genes of HeLa cells on the micropillar array.

Note:

Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway is a collection of

manually drawn pathway maps representing human's knowledge on the molecular interaction, reaction and relation networks [S3]. The pathways are classified into seven categories including metabolism, genetic information processing, environmental information processing, cellular processes, organismal systems, human diseases, and drug development. The drug development category is not concerned in the present work. Each category is further detailed into three levels (level 2, level 3 and level 4): level 2 is so far composed of 57 pathways; level 3 shows the metabolic pathway maps under level 2; level 4 interprets the concrete legends of each metabolic pathway map. The differentially expressed genes are classified in the level 2 subcategories.

Table S1. Up-regulated genes of HeLa cells on the micropillar array *versus* on the smooth surface

No.	Gene Symbol	Description	No.	Gene Symbol	Description
1	HOXA3	homeobox A3	91	GATA2	GATA binding protein 2
2	DSC2	desmocollin 2	92	PLEKHM3	pleckstrin homology domain containing, family M, member 3
3	TCN1	transcobalamin I (vitamin B12 binding protein, R binder family)	93	SPTLC3	serine palmitoyltransferase, long chain base subunit 3
4	FABP7	fatty acid binding protein 7, brain	94	ACOXL	acyl-CoA oxidase-like
5	MGP	matrix Gla protein	95	KIF5C	kinesin family member 5C
6	KCTD16	potassium channel tetramerization domain containing 16	96	FENDRR	FOXF1 adjacent non-coding developmental regulatory RNA
7	TYRP1	tyrosinase-related protein 1	97	RFPL3S	RFPL3 antisense
8	YPEL3	yippee-like 3 (Drosophila)	98	SNORD113-3	small nucleolar RNA, C/D box 113-3
9	AMTN	amelotin	99	LSM14A	LSM14A, SCD6 homolog A (S. cerevisiae)
10	CFB	complement factor B	100	DST	dystonin
11	RHEBL1	Ras homolog enriched in brain like 1	101	TBC1D3B	TBC1 domain family, member 3B
12	LOC143666	uncharacterized LOC143666	102	CAMKK1	calcium/calmodulin-dependent protein kinase 1, alpha
13	MLLT6	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 6	103	ADRA2A	adrenoceptor alpha 2A
14	GDF15	growth differentiation factor 15	104	IGFBP5	insulin-like growth factor binding protein 5
15	CES1	carboxylesterase 1	105	PI16	peptidase inhibitor 16
16	BCL2L11	BCL2-like 11 (apoptosis facilitator)	106	ADAMTS10	ADAM metallopeptidase with thrombospondin type 1 motif, 10
17	B3GAT3	beta-1,3-glucuronyltransferase 3	107	FAM102A	family with sequence similarity 102, member A
18	C1orf21	chromosome 1 open reading frame 21	108	RDX	radixin
19	PXMP2	peroxisomal membrane protein 2, 22kDa	109	VGLL4	vestigial-like family member 4
20	SNAI3-AS1	SNAI3 antisense RNA 1	110	LOC100507564	uncharacterized LOC100507564
21	RN7SK	RNA, 7SK small nuclear	111	KCNK2	potassium channel, two pore domain subfamily K, member 2
22	OLFM1	olfactomedin 1	112	CTSF	cathepsin F

23	FAM13A-AS1	FAM13A antisense RNA 1	113	PCSK1	proprotein convertase subtilisin/kexin type 1
24	IDUA	iduronidase, alpha-L-	114	CTNNBIP1	catenin, beta interacting protein 1
25	LY6D	lymphocyte antigen 6 complex, locus D	115	TRPM6	transient receptor potential cation channel, subfamily M, member 6
26	ANGPTL4	angiopoietin-like 4	116	ANGPT1	angiopoietin 1
27	CD36	CD36 molecule (thrombospondin receptor)	117	TNFRSF11B	tumor necrosis factor receptor superfamily, member 11b
28	CYP27C1	cytochrome P450, family 27, subfamily C, polypeptide 1	118	TBXAS1	thromboxane A synthase 1 (platelet)
29	BBC3	BCL2 binding component 3	119	LHPP	phosphohistidine phosphatase
30	ITGA11	integrin, alpha 11	120	DLX3	distal-less homeobox 3
31	ST6GALNA C2	ST6 (alpha-N-acetyl-neuraminyl-2,3-beta-galactosyl-1,3)-N-acetylgalactosaminide alpha-2,6-sialyltransferase 2	121	C3	complement component 3
32	STOX1	storkhead box 1	122	GATA2-AS1	GATA2 antisense RNA 1
33	SESTD1	SEC14 and spectrin domains 1	123	ETV1	ets variant 1
34	ALDH7A1	aldehyde dehydrogenase 7 family, member A1	124	TSL	testis-expressed, seven-twelve, leukemia
35	MEX3A	mex-3 RNA binding family member A	125	CXXC4	CXXC finger protein 4
36	CORO7	coronin 7	126	MRPS31P5	mitochondrial ribosomal protein S31 pseudogene 5
37	TCERG1L-AS1	TCERG1L antisense RNA 1	127	TXNIP	thioredoxin interacting protein
38	MTUS2	microtubule associated tumor suppressor candidate 2	128	SSC5D	scavenger receptor cysteine rich family, 5 domains
39	MTR	5-methyltetrahydrofolate-homocysteine methyltransferase	129	SCN1A	sodium channel, voltage gated, type I alpha subunit
40	CAPN5	calpain 5	130	ABCC3	ATP-binding cassette, sub-family C (CFTR/MRP), member 3
41	CARD6	caspase recruitment domain family, member 6	131	SLC44A5	solute carrier family 44, member 5
42	FAM78A	family with sequence similarity 78, member A	132	FCGR2A	Fc fragment of IgG, low affinity IIa, receptor (CD32)
43	LINC01563	long intergenic non-protein coding RNA 1563	133	C5	complement component 5
44	ODAM	odontogenic, ameloblast associated	134	UACA	uveal autoantigen with coiled-coil domains and ankyrin repeats

45	SYNE2	spectrin repeat containing, nuclear envelope 2	135	GATS	GATS, stromal antigen 3 opposite strand
46	OR2M7	olfactory receptor, family 2, subfamily M, member 7	136	GPER1	G protein-coupled estrogen receptor 1
47	MYB	v-myb avian myeloblastosis viral oncogene homolog	137	PLCXD3	phosphatidylinositol-specific phospholipase C, X domain containing 3
48	SRPX2	sushi-repeat containing protein, X-linked 2	138	LFNG	LFNG O-fucosylpeptide 3-beta-N-acetylglucosaminyltransferase
49	GTF3C5	general transcription factor IIIC, polypeptide 5, 63kDa	139	NUPR1	nuclear protein, transcriptional regulator, 1
50	DAPL1	death associated protein-like 1	140	SMPDL3A	sphingomyelin phosphodiesterase, acid-like 3A
51	ETV5	ets variant 5	141	CCDC74B	coiled-coil domain containing 74B
52	LOC101930114	uncharacterized LOC101930114	142	ACADL	acyl-CoA dehydrogenase, long chain
53	C3orf80	chromosome 3 open reading frame 80	143	AMY1C	amylase, alpha 1C (salivary)
54	SMAD9	SMAD family member 9	144	ISLR	immunoglobulin superfamily containing leucine-rich repeat
55	TMSB15A	thymosin beta 15a	145	RHBDL3	rhomboid, veinlet-like 3 (Drosophila)
56	GPR98	G protein-coupled receptor 98	146	MECOM	MDS1 and EVI1 complex locus
57	SPOCK3	sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 3	147	KLHL24	kelch-like family member 24
58	BMF	Bcl2 modifying factor	148	SCARA5	scavenger receptor class A, member 5
59	RAB17	RAB17, member RAS oncogene family	149	MEF2C	myocyte enhancer factor 2C
60	STXBP5L	syntaxin binding protein 5-like	150	MTURN	maturin, neural progenitor differentiation regulator homolog (Xenopus)
61	LOC284600	uncharacterized LOC284600	151	LDLRAD4	low density lipoprotein receptor class A domain containing 4
62	PRRT2	proline-rich transmembrane protein 2	152	CDC42BPG	CDC42 binding protein kinase gamma (DMPK-like)
63	BZRAP1	benzodiazepine receptor (peripheral) associated protein 1	153	LOC284014	uncharacterized LOC284014
64	ZNF395	zinc finger protein 395	154	DLX5	distal-less homeobox 5
65	FSIP2	fibrous sheath interacting protein 2	155	UNC5B	unc-5 homolog B (C. elegans)
66	MIR181A1H	MIR181A1 host gene (non-protein coding)	156	GTF2IRD2	GTF2I repeat domain containing 2

67	GAS6-AS1	GAS6 antisense RNA 1	157	C5orf58	chromosome 5 open reading frame 58
68	CCDC7	coiled-coil domain containing 7	158	LOC101927196	uncharacterized LOC101927196
69	EWSAT1	Ewing sarcoma associated transcript 1	159	ST6GAL1	ST6 beta-galactosamide alpha-2,6-sialyltranferase 1
70	MFAP4	microfibrillar-associated protein 4	160	SLC37A2	solute carrier family 37 (glucose-6-phosphate transporter), member 2
71	SNHG23	small nucleolar RNA host gene 23 (non-protein coding)	161	ALDH3A1	aldehyde dehydrogenase 3 family, member A1
72	FCGR2C	Fc fragment of IgG, low affinity IIc, receptor for (CD32) (gene/pseudogene)	162	LOC101928617	uncharacterized LOC101928617
73	SMC1A	structural maintenance of chromosomes 1A	163	C4BPA	complement component 4 binding protein, alpha
74	CACNA1G	calcium channel, voltage-dependent, T type, alpha 1G subunit	164	ARRDC2	arrestin domain containing 2
75	SCARF2	scavenger receptor class F, member 2	165	VIPR2	vasoactive intestinal peptide receptor 2
76	NTNG1	netrin G1	166	ATG16L2	autophagy related 16-like 2 (S. cerevisiae)
77	TNFSF4	tumor necrosis factor (ligand) superfamily, member 4	167	TTLL1	tubulin tyrosine ligase-like family member 1
78	DOK5	docking protein 5	168	SNCAIP	synuclein, alpha interacting protein
79	SMURF2	SMAD specific E3 ubiquitin protein ligase 2	169	SYT2	synaptotagmin II
80	KLF3-AS1	KLF3 antisense RNA 1	170	MOGAT3	monoacylglycerol O-acyltransferase 3
81	C1R	complement component 1, r subcomponent	171	C1QTNF1	C1q and tumor necrosis factor related protein 1
82	DAPK2	death-associated protein kinase 2	172	CFAP44	cilia and flagella associated protein 44
83	C19orf57	chromosome 19 open reading frame 57	173	FZD10	frizzled class receptor 10
84	MEG3	maternally expressed 3 (non-protein coding)	174	DDR1	discoidin domain receptor tyrosine kinase 1
85	PGAP3	post-GPI attachment to proteins 3	175	ANO3	anoctamin 3
86	TRIM34	tripartite motif containing 34	176	HLA-DRB5	major histocompatibility complex, class II, DR beta 5
87	RPS6KA5	ribosomal protein S6 kinase, 90kDa, polypeptide 5	177	NME8	NME/NM23 family member 8
88	AKR1C1	aldo-keto reductase family 1,	178	SNORD114-1	small nucleolar RNA, C/D box

		member C1		1	114-11
89	GAA	glucosidase, alpha; acid	179	LOC1009962 49	uncharacterized LOC100996249
90	DUSP26	dual specificity phosphatase 26 (putative)	180	FAM13C	family with sequence similarity 13, member C

- Highlight texts in bright blue represent the noncoding RNA genes.
- Highlight texts in gray represent the pseudo genes.
- Highlight texts in green represent the non-annotated genes.

Table S2. Down-regulated genes of HeLa cells on the micropillar array *versus* on the smooth surface

No.	Gene Symbol	Description	No.	Gene Symbol	Description
1	MMP23B	matrix metallopeptidase 23B	129	TNC	tenascin C
2	RGS5	regulator of G-protein signaling 5	130	PKP2	plakophilin 2
3	ERV MER34-1	endogenous retrovirus group MER34, member 1	131	PTPRQ	protein tyrosine phosphatase, receptor type, Q
4	JAG1	jagged 1	132	STXBP6	syntaxin binding protein 6 (amisyn)
5	RNF144B	ring finger protein 144B	133	MMP24	matrix metallopeptidase 24 (membrane-inserted)
6	SDC2	syndecan 2	134	CLDN11	claudin 11
7	SNAR-I	small ILF3/NF90-associated RNA A3	135	GSTM2	glutathione S-transferase mu 2 (muscle)
8	IGFBP1	insulin-like growth factor binding protein 1	136	FRMD5	FERM domain containing 5
9	HIVEP3	human immunodeficiency virus type I enhancer binding protein 3	137	ATP6V0A4	ATPase, H ⁺ transporting, lysosomal V0 subunit a4
10	IFI44	interferon-induced protein 44	138	ACTA2	actin, alpha 2, smooth muscle, aorta
11	TGM1	transglutaminase 1	139	ADM	adrenomedullin
12	PRB4	proline-rich protein BstNI subfamily 4	140	BMP4	bone morphogenetic protein 4
13	PTGER4	prostaglandin E receptor 4 (subtype EP4)	141	SYNPO	synaptopodin
14	AREG	amphiregulin	142	TNNT2	troponin T type 2 (cardiac)
15	PIP5K1B	phosphatidylinositol-4-phosphate 5-kinase, type I, beta	143	MYL9	myosin, light chain 9, regulatory
16	TENM2	teneurin transmembrane protein 2	144	CPA4	carboxypeptidase A4
17	LINC00525	long intergenic non-protein coding RNA 525	145	WNT7B	wingless-type MMTV integration site family, member 7B
18	VLDLR-AS1	VLDLR antisense RNA 1	146	SLC2A14	solute carrier family 2 (facilitated glucose transporter), member 14
19	DACT1	dishevelled-binding antagonist of beta-catenin 1	147	MYL2	myosin, light chain 2, regulatory, cardiac, slow
20	GPAT2	glycerol-3-phosphate acyltransferase 2, mitochondrial	148	SLC2A3	solute carrier family 2 (facilitated glucose transporter), member 3
21	FAM200B	family with sequence similarity 200, member B	149	SUSD2	sushi domain containing 2
22	SDPR	serum deprivation response	150	TAGLN	transgelin
23	EPPK1	epiplakin 1	151	NUAK2	NUAK family, SNF1-like kinase, 2
24	TRPC4	transient receptor potential cation channel, subfamily C, member 4	152	CRABP2	cellular retinoic acid binding protein 2

25	MSRB3	methionine sulfoxide reductase B3	153	ANXA3	annexin A3
26	GIT2	G protein-coupled receptor kinase interacting ArfGAP 2	154	LGSN	lengsin, lens protein with glutamine synthetase domain
27	ZDHHC11	zinc finger, DHHC-type containing 11	155	PADI1	peptidyl arginine deiminase, type I
28	SLC2A5	solute carrier family 2 (facilitated glucose/fructose transporter), member 5	156	PLEKHA7	pleckstrin homology domain containing, family A member 7
29	CFAP45	cilia and flagella associated protein 45	157	PLAC8	placenta-specific 8
30	MKRN9P	makorin ring finger protein 9, pseudogene	158	TM4SF1-AS1	TM4SF1 antisense RNA 1
31	CHIC1	cysteine-rich hydrophobic domain 1	159	DKK1	dickkopf WNT signaling pathway inhibitor 1
32	FHDC1	FH2 domain containing 1	160	LINC01186	long intergenic non-protein coding RNA 1186
33	AFAP1	actin filament associated protein 1	161	MFAP5	microfibrillar associated protein 5
34	NPR3	natriuretic peptide receptor 3	162	CAPSL	calcyphosine-like
35	DDAH1	dimethylarginine dimethylaminohydrolase 1	163	KRT80	keratin 80, type II
36	CAV3	caveolin 3	164	EHD4	EH-domain containing 4
37	DNER	delta/notch-like EGF repeat containing	165	HBEGF	heparin-binding EGF-like growth factor
38	SPEF2	sperm flagellar 2	166	IGFBP3	insulin-like growth factor binding protein 3
39	CCNA1	cyclin A1	167	ACTG2	actin, gamma 2, smooth muscle, enteric
40	ZNF365	zinc finger protein 365	168	MOB3B	MOB kinase activator 3B
41	GBP1	guanylate binding protein 1, interferon-inducible	169	TACSTD2	tumor-associated calcium signal transducer 2
42	NEXN	nexilin (F actin binding protein)	170	KRT4	keratin 4, type II
43	GPR126	G protein-coupled receptor 126	171	ANO2	anoctamin 2, calcium activated chloride channel
44	CAV1	caveolin 1, caveolae protein, 22kDa	172	C11orf96	chromosome 11 open reading frame 96
45	MYO7A	myosin VIIA	173	C1orf116	chromosome 1 open reading frame 116
46	AOX1	aldehyde oxidase 1	174	XPO6	exportin 6
47	IL18	interleukin 18	175	BCL2L1	BCL2-like 1
48	CELF2	CUGBP, Elav-like family member 2	176	CITED2	Cbp/p300-interacting transactivator, with Glu/Asp-rich carboxy-terminal domain, 2
49	MPP7	membrane protein, palmitoylated 7	177	A1BG	alpha-1-B glycoprotein

		(MAGUK p55 subfamily member 7)			
50	ADAMTS1	ADAM metallopeptidase with thrombospondin type 1 motif, 1	178	EVA1A	eva-1 homolog A (<i>C. elegans</i>)
51	FLVCR2	feline leukemia virus subgroup C cellular receptor family, member 2	179	HSPB2	heat shock 27kDa protein 2
52	FRAS1	Fraser extracellular matrix complex subunit 1	180	DUSP1	dual specificity phosphatase 1
53	JPH2	junctophilin 2	181	KLLN	killin, p53-regulated DNA replication inhibitor
54	HS3ST3B1	heparan sulfate (glucosamine) 3-O-sulfotransferase 3B1	182	IL6	interleukin 6
55	TLE4	transducin-like enhancer of split 4	183	CTGF	connective tissue growth factor
56	NTN4	netrin 4	184	LOC100506271	uncharacterized LOC100506271
57	FBLIM1	filamin binding LIM protein 1	185	CASZ1	castor zinc finger 1
58	TIAM2	T-cell lymphoma invasion and metastasis 2	186	SNTB1	syntrophin, beta 1 (dystrophin-associated protein A1, 59kDa, basic component 1)
59	CDS1	CDP-diacylglycerol synthase (phosphatidate cytidylyltransferase) 1	187	SP6	Sp6 transcription factor
60	ANKRD2	ankyrin repeat domain 2 (stretch responsive muscle)	188	TRNP1	TMF1-regulated nuclear protein 1
61	PRICKLE1	prickle homolog 1 (<i>Drosophila</i>)	189	SNORA12	small nucleolar RNA, H/ACA box 12
62	ALPK2	alpha-kinase 2	190	LINC00421	long intergenic non-protein coding RNA 421
63	NT5E	5'-nucleotidase, ecto (CD73)	191	RBM24	RNA binding motif protein 24
64	ANKRD33B	ankyrin repeat domain 33B	192	NETO1	neuropilin (NRP) and tolloid (TLL)-like 1
65	MIR143HG	MIR143 host gene (non-protein coding)	193	RTKN2	rhotekin 2
66	ALPP	alkaline phosphatase, placental	194	ZBED2	zinc finger, BED-type containing 2
67	RNF223	ring finger protein 223	195	CGN	cingulin
68	KRT16P2	keratin 16 pseudogene 2	196	SAMD4A	sterile alpha motif domain containing 4A
69	FLNA	filamin A, alpha	197	TMEM139	transmembrane protein 139
70	FAM124A	family with sequence similarity 124A	198	IL7R	interleukin 7 receptor
71	ITGBLA	integrin, beta-like 1 (with EGF-like repeat domains)	199	ATP8B1	ATPase, aminophospholipid transporter, class I, type 8B, member 1
72	RNASE4	ribonuclease, RNase A family, 4	200	ULK4	unc-51 like kinase 4

73	INO80C	INO80 complex subunit C	201	EDN1	endothelin 1
74	KCNH1-IT1	KCNH1 intronic transcript 1 (non-protein coding)	202	LINC00052	long intergenic non-protein coding RNA 52
75	IGFL1	IGF-like family member 1	203	NEK6	NIMA-related kinase 6
76	P2RY2	purinergic receptor P2Y, G-protein coupled, 2	204	MYLK	myosin light chain kinase
77	NOXO1	NADPH oxidase organizer 1	205	CSRP1	cysteine and glycine-rich protein 1
78	LOC1027238 34	uncharacterized LOC102723834	206	NXN	nucleoredoxin
79	NID2	nidogen 2 (osteonidogen)	207	SSR4P1	signal sequence receptor, delta pseudogene 1
80	SERTAD4-A S1	SERTAD4 antisense RNA 1	208	GPR20	G protein-coupled receptor 20
81	MOSPD1	motile sperm domain containing 1	209	ICAM1	intercellular adhesion molecule 1
82	NRG1	neuregulin 1	210	CYR61	cysteine-rich, angiogenic inducer, 61
83	KIR2DS4	killer cell immunoglobulin-like receptor, two domains, short cytoplasmic tail, 4	211	AJUBA	ajuba LIM protein
84	RIMKLB	ribosomal modification protein rimK-like family member B	212	GPRC5A	G protein-coupled receptor, class C, group 5, member A
85	SYNE1-AS1	SYNE1 antisense RNA 1	213	LINC00668	long intergenic non-protein coding RNA 668
86	LOC729870	uncharacterized LOC729870	214	LINC00570	long intergenic non-protein coding RNA 570
87	PHLDB2	pleckstrin homology-like domain, family B, member 2	215	HTR1D	5-hydroxytryptamine (serotonin) receptor 1D, G protein-coupled
88	PTPLB	protein tyrosine phosphatase-like (proline instead of catalytic arginine), member b	216	EMP1	epithelial membrane protein 1
89	TM4SF1	transmembrane 4 L six family member 1	217	LOC283140	uncharacterized LOC283140
90	RAB20	RAB20, member RAS oncogene family	218	MROH1	maestro heat-like repeat family member 1
91	C1orf167	chromosome 1 open reading frame 167	219	LOC100505817 17	uncharacterized LOC100505817
92	EGR1	early growth response 1	220	F3	coagulation factor III (thromboplastin, tissue factor)
93	INSL4	insulin-like 4 (placenta)	221	AP1M2	adaptor-related protein complex 1, mu 2 subunit
94	RBP7	retinol binding protein 7, cellular	222	TNNC1	troponin C type 1 (slow)
95	FAM189A2	family with sequence similarity 189, member A2	223	LIMS2	LIM and senescent cell antigen-like domains 2
96	NEDD9	neural precursor cell expressed,	224	MYPN	myopalladin

		developmentally down-regulated 9			
97	GACAT2	gastric cancer associated transcript 2 (non-protein coding)	225	ARHGAP28	Rho GTPase activating protein 28
98	CRB1	crumbs family member 1, photoreceptor morphogenesis associated	226	UCA1	urothelial cancer associated 1 (non-protein coding)
99	ZNF316	zinc finger protein 316	227	CDC42EP2	CDC42 effector protein (Rho GTPase binding) 2
100	SNAR-H	small ILF3/NF90-associated RNA I	228	LOC100268168	uncharacterized LOC100268168
102	SNAR-G1	small ILF3/NF90-associated RNA G2	229	TCP11L1	t-complex 11, testis-specific-like 1
102	SNAR-G2	small ILF3/NF90-associated RNA H	230	MAPK4	mitogen-activated protein kinase 4
103	HDC	histidine decarboxylase	231	EFEMP1	EGF containing fibulin-like extracellular matrix protein 1
104	SPANXB1	SPANX family, member B1	232	KLHL29	kelch-like family member 29
105	SNAR-F	small ILF3/NF90-associated RNA G1	233	C1orf198	chromosome 1 open reading frame 198
106	SNAR-B2	small ILF3/NF90-associated RNA F	234	ROR1	receptor tyrosine kinase-like orphan receptor 1
107	SNAR-A3	small ILF3/NF90-associated RNA B2	235	REEP2	receptor accessory protein 2
108	LETM2	leucine zipper-EF-hand containing transmembrane protein 2	236	BDNF	brain-derived neurotrophic factor
109	PLEKHG1	pleckstrin homology domain containing, family G (with RhoGef domain) member 1	237	TUFT1	tuftelin 1
110	PLCB4	phospholipase C, beta 4	238	LIMA1	LIM domain and actin binding 1
111	TMEM125	transmembrane protein 125	239	HHIP	hedgehog interacting protein
112	KRT13	keratin 13, type I	240	ENPP1	ectonucleotide pyrophosphatase/phosphodiesterase 1
113	RGS11	regulator of G-protein signaling 11	241	ANKRD1	ankyrin repeat domain 1 (cardiac muscle)
114	TSPAN13	tetraspanin 13	242	COL16A1	collagen, type XVI, alpha 1
115	H19	H19, imprinted maternally expressed transcript (non-protein coding)	243	KLC3	kinesin light chain 3
116	MEOX1	mesenchyme homeobox 1	244	HS1BP3	HCLS1 binding protein 3
117	TPM1	tropomyosin 1 (alpha)	245	OLR1	oxidized low density lipoprotein (lectin-like) receptor 1
118	CAV2	caveolin 2	246	P3H2	prolyl 3-hydroxylase 2
119	ADAMTSL1	ADAMTS-like 1	247	TRIML2	tripartite motif family-like 2

120	DUSP5	dual specificity phosphatase 5	248	ADAMTS8	ADAM metallopeptidase with thrombospondin type 1 motif, 8
121	KRT17	keratin 17, type I	249	MTMR1	myotubularin related protein 1
122	LOC1005056 64	uncharacterized LOC100505664	250	STX11	syntaxin 11
123	CARD9	caspase recruitment domain family, member 9	251	C10orf54	chromosome 10 open reading frame 54
124	KRT14	keratin 14, type I	252	SEMA3D	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3D
125	KRT18P55	keratin 18 pseudogene 55	253	SPANXC	SPANX family, member C
126	TGM2	transglutaminase 2	254	ERC	ELKS/RAB6-interacting/CAST family member 2
127	SV2B	synaptic vesicle glycoprotein 2B	255	LRRC15	leucine rich repeat containing 15
128	FAM46B	family with sequence similarity 46, member B			

- Highlight texts in bright blue represent the noncoding RNA genes.
- Highlight texts in gray represent the pseudo genes.

Table S3. Differentially expressed genes of HeLa cells on the micropillar array related to the level 3 pathways of signal transduction

Level 3 pathway of signal transduction	Gene number	Up-regulated genes	Down-regulated genes
Ras signaling pathway	3	ANGPT1	BDNF BCL2L1
Rap1 signaling pathway	2	ANGPT1	PLCB4
MAPK signaling pathway	10	CACNA1G ANGPT1 RPS6KA5 MECOM MEF2C	BDNF DUSP5 AREG DUSP1 FLNA
ErbB signaling pathway	3	-	NRG1 AREG HBEGF
Wnt signaling pathway	8	CXXC4 FZD10 CTNNBIP1	ROR1 PLCB4 WNT7B DKK1 PRICKLE1
Notch signaling pathway	2	LFNG	JAG1
Hedgehog signaling pathway	2	SMURF2	HHIP
TGF-beta signaling pathway	3	SMAD9 SMURF2	BMP4
Hippo signaling pathway	8	BBC3 FZD10	AREG WNT7B CRB1 BMP4 CTGF AJUBA
Hippo signaling pathway - multiple species	1	-	AJUBA
Apelin signaling pathway	8	MEF2C	JAG1 EGR1 ACTA2 MYLK PLCB4 CTGF MYL2
NF-kappa B signaling pathway	2	-	BCL2L1 ICAM1
TNF signaling pathway	5	RPS6KA5	JAG1 ICAM1 EDN1 IL6
HIF-1 signaling pathway	3	ANGPT1	EDN1 IL6
FoxO signaling pathway	3	BCL2L11	IL7R IL6
Calcium signaling pathway	4	CACNA1G	MYLK PLCB4 TNNC1
Phosphatidylinositol signaling system	4	-	PIP5K1B MTMR1 PLCB4 CDS1
Phospholipase D signaling pathway	2	-	PIP5K1B PLCB4
Sphingolipid signaling pathway	2	SPTLC3	PLCB4
cAMP signaling pathway	6	VIPR2	HTR1D BDNF MYL9 EDN1 HHIP
cGMP-PKG signaling pathway	5	MEF2C ADRA2A	MYL9 MYLK PLCB4
PI3K-Akt signaling pathway	10	ANGPT1 ITGA11 BCL2L11 MYB	BDNF IL7R BCL2L1 AREG TNC IL6
AMPK signaling pathway	2	CD36	CCNA1
mTOR signaling pathway	2	FZD10	WNT7B

“-”means that no differentially expressed genes was detected in the pathway.

Table S4. Positions of the genes of MAPK and PI3K-Akt signaling pathways on the chromosomes of HeLa cells on the PLGA micropillar array

Level 3 pathway of signal transduction	Up-regulated genes	Position	Down-regulated genes	Position
MAPK signaling pathway	CACNA1G	17q21.33	BDNF	11p14.1
	ANGPT1	8q23.1	DUSP5	10q25.2
	RPS6KA5	14q32.11	AREG	4q13.3
	MECOM	3q26.2	DUSP1	5q35.1
PI3K-Akt signaling pathway	MEF2C	5q14.3	FLNA	Xq28
	ANGPT1	8q23.1	BDNF	11p14.1
	ITGA11	15q23	IL7R	5p13.2
	BCL2L11	2q13	BCL2L1	20q11.21
	MYB	6q23.3	AREG	4q13.3
			TNC	9q33.1
			IL6	7p15.3

- In the columns of “Up-regulated genes” and “Down-regulated genes”, the yellow color indicates the differentially expressed genes existed in both signaling pathways.
- In the column of “Position”, “p” denotes a short arm, and “q” defers to a long arm; the position “17q21.33” of CACNA1G means that the CACNA1G gene on the long arm (p) of chromosome 17 was found at the band labeled 21.33, and the other symbols indicate similar meanings. Here, the presentation sequence for the same pathway in the column of “Position” follows that of the corresponding genes appeared in Fig. 5C.

Table S5. GO and KEGG classifications of differentially expressed genes on chromosome 18

GeneSymbol	Regulation	GO term in Figure 7	KEGG pathway in Figure 7
LINC00668	down	-	-
ARHGAP28	down	2, 3, 7, 15, 17, 33, 36, 37, 47, 50, 53, 55	-
LDLRAD4	up	2, 15, 17, 21, 22, 23, 24, 25, 33, 36, 37, 39, 42, 43, 44, 45, 47, 50, 53, 55	-
DSC2	up	2, 15, 16, 17, 18, 19, 21, 22, 24, 32, 33, 37, 39, 42, 45, 50, 53, 55	32
INO80C	down	15, 17, 20, 23, 24, 25, 36, 37, 44, 53	-
MAPK4	down	2, 3, 10, 15, 17, 23, 24, 25, 33, 37, 44, 50, 53, 55	18
GACAT2	down	-	-
ATP8B1	down	2, 3, 14, 15, 17, 21, 22, 24, 25, 33, 36, 37, 42, 44, 45, 47, 50, 53	-
ALPK2	down	2, 3, 37, 44	-
NETO1	down	2, 8, 10, 14, 15, 16, 17, 18, 21, 22, 24, 25, 29, 30, 31, 33, 37, 42, 45, 48, 50, 53, 55	-
LOC100505817	down	-	-

- “-” means not detected in either GO or KEGG pathway databases.
- Highlight texts in bright blue color represent the noncoding RNA genes.
- GO term: 1-14, Molecular Function; 15-30, Cellular Component; 31-55, Biological Process.
- KEGG pathway: 1-9, Metabolism; 10, Genetic Information Processing; 11-13, Environmental Information Processing; 14-17, Cellular Processes; 18-26, Organism Systems; 27-37, Human Diseases.

Table S6. GO and KEGG classifications of differentially expressed genes on chromosome 19

GeneSymbol	Regulation	GO term in Figure 7	KEGG pathway in Figure 7
C3	up	2, 3, 7, 14, 15, 17, 18, 19, 20, 21, 22, 23, 24, 25, 28, 33, 36, 37, 39, 41, 42, 44, 45, 46, 47, 48, 50, 53, 55	3, 11, 12, 13, 14, 15, 21, 30, 27, 28, 29, 30, 34, 35, 36, 37
ANGPTL4	up	2, 3, 7, 18, 19, 33, 36, 37, 39, 44, 45, 47, 48, 50, 53	19, 21
ADAMTS10	up	2, 3, 18, 19, 28, 44	-
ICAM1	down	2, 3, 8, 9, 10, 15, 16, 17, 18, 19, 21, 22, 24, 32, 33, 35, 36, 37, 39, 41, 42, 43, 44, 45, 46, 47, 48, 50, 51, 52, 53, 54, 55	12, 13, 18, 29, 32, 33, 34, 35, 36,
AP1M2	down	2, 15, 17, 20, 21, 22, 24, 25, 37, 41, 42, 46	14, 35
C19orf57	up	2, 39, 45	-
UCA1	down	33, 44, 50	-
ARRDC2	up	15, 17, 21, 24	-
GDF15	up	2, 3, 7, 8, 10, 15, 17, 18, 19, 24, 31, 33, 36, 37, 39, 40, 44, 45, 47, 48, 50, 53, 55	13
LSM14A	up	2, 15, 17, 20, 24, 33, 36, 37, 39, 41, 44, 45, 46, 48, 50, 53, 55	-
KLC3	down	2, 3, 15, 17, 20, 24, 25, 28, 37, 42	34
IGFL1	down	2, 18, 19	-
BBC3	up	2, 3, 15, 17, 24, 33, 36, 37, 42, 44, 48, 50, 53, 55	12, 15, 27, 28, 30, 35, 37
SNAR-A3	down	15, 17, 24	-
SNAR-G2	down	15, 17, 24	-
SNAR-G1	down	-	-
SNAR-B2	down	15, 17, 24	-
SNAR-F	down	-	-
KIR2DS4	down	2, 15, 17, 21, 22, 41, 53	18
SSC5D	up	2, 8, 15, 17, 18, 19, 21, 22, 33, 37, 39, 41, 42, 45, 46, 47, 50, 53	-
A1BG	down	15, 17, 18, 19, 23, 24, 25, 37, 41, 42, 53	-

“-” means not detected in either GO or KEGG pathway databases.

Highlight texts in bright blue represent the noncoding RNA genes.

GO term: **1-14**, Molecular Function; **15-30**, Cellular Component; **31-55**, Biological Process.

KEGG pathway: **1-9**, Metabolism; **10**, Genetic Information Processing; **11-13**, Environmental Information Processing; **14-17**, Cellular Processes; **18-26**, Organism Systems; **27-37**, Human Diseases.

Table S7. Top 30 of GO enrichment of differentially expressed genes of HeLa cells on the micropillar array

No.	GO terms	TYPE	Gene Ratio	Bg Ratio	p value	q value	Genes	Enrichment factor
1	HMG box domain binding	Molecular function	4/376	16/20400	6.2E-05	0.0028	HOXA3, MEOX1, MEF2C, DLX5	13.56
2	regulation of urine volume	Biological process	4/376	21/20400	0.00019	0.0060	ADM, NPR3, EDN1, MLLT6	10.33
3	wound healing, spreading of cells	Biological process	6/376	32/20400	1.2E-05	0.0009	DDR1, FLNA, CYR61, AJUBA, PHLDB2, HBEGF	10.17
4	fibronectin binding	Molecular function	5/376	27/20400	5.1E-05	0.0025	IGFBP3, SSC5D, LRRC15, CTGF, IGFBP5	10.05
5	regulation of odontogenesis	Biological process	5/376	27/20400	5.1E-05	0.0025	TNFRSF11B, EDN1, BMP4, AMTN, SP6	10.05
6	intermediate filament organization	Biological _process	4/376	22/20400	0.00023	0.0069	EPPK1, KRT14, KLHL24, PKP2	9.86
7	insulin-like growth factor binding	Molecular function	5/376	28/20400	6.1E-05	0.0028	IGFBP3, CYR61, IGFBP5, IGFBP1, CTGF	9.69
8	glomerulus vasculature development	Biological process	4/376	25/20400	0.00038	0.0096	EGR1, ACTA2, BMP4, ANGPT1	8.68
9	negative regulation of myoblast differentiation	Biological process	4/376	25/20400	0.00038	0.0096	PRICKLE1, IL18, ANKRD2, BMP4	8.68
10	branching involved in mammary gland duct morphogenesis	Biological process	4/376	25/20400	0.00038	0.0096	AREG, ETV5, CAV3, DDR1	8.68
11	mammary gland morphogenesis	Biological process	7/376	46/20400	1.1E-05	0.00093	BMP4, IGFBP5, CAV3, AREG, ETV5, CAV1, DDR1	8.26
12	regulation of cardiac muscle	Biological process	5/376	34/20400	0.00016	0.0054	PKP2, FLNA, CAV1, DSC2,	7.98

	cell action potential						CAV3	
13	regulation of the force of heart contraction	Biological process	4/376	28/20400	0.00060	0.014	ADM, MYL2, CAV1, GAA	7.75
14	sarcomere organization	Biological process	7/376	49/20400	1.7E-05	0.0012	EDN1, TPM1, MYPN, MEF2C, TNNT2, CAV3, ANKRD1	7.75
15	intestinal absorption	Biological process	5/376	35/20400	0.00018	0.0061	CD36, ADRA2A, AKR1C1, SLC2A5, LIMA1	7.75
16	cell-cell adhesion mediator activity	Molecular function	7/376	50/20400	2.0E-05	0.0014	STXBP6, NEXN, MYPN, NTNG1, PKP2, TACSTD2, DSC2	7.6
17	laminin binding	Molecular function	4/376	29/20400	0.00070	0.014	LRRC15, SSC5D, GPR126, NTN4	7.48
18	positive regulation of cardiac muscle cell differentiation	Biological process	4/376	29/20400	0.00070	0.014	EDN1, BMP4, MEF2C, NRG1	7.48
19	positive regulation of release of cytochrome c from mitochondria	Biological process	4/376	30/20400	0.00080	0.015	BCL2L11, BBC3, GPER1, BMF	7.23
20	regulation of ruffle assembly	Biological process	4/376	30/20400	0.00080	0.015	RDX, CAV1, ICAM1, TACSTD2	7.23
21	regulation of myoblast differentiation	Biological process	7/376	53/20400	2.9E-05	0.0017	IGFBP3, ANKRD2, BMP4, IL18, RBM24, PRICKLE1, MEF2C	7.17
22	ventricular cardiac muscle tissue morphogenesis	Biological process	6/376	47/20400	0.00011	0.0042	TNNC1, PKP2, TPM1, MYL2, NRG1, TNNT2	6.93
23	regulation of collagen metabolic	Biological process	6/376	48/20400	0.00012	0.0045	IL6, CTGF, MFAP4, BMP4, C10ORF54, MYB	6.78

	process							
24	morphogenesis of an epithelial sheet	Biological process	7/376	56/20400	4.1E-05	0.0022	CYR61, FLNA, HBEGF, PHLDB2, AJUBA, DDR1, JAG1	6.78
25	cardiac muscle cell action potential involved in contraction	Biological process	7/376	56/20400	4.1E-05	0.0022	SCN1A, CAV3, CAV1, FLNA, DSC2, PKP2, CACNA1G	6.78
26	cardiac ventricle morphogenesis	Biological process	9/376	73/20400	5.5E-06	0.00051	TNNC1, JAG1, TPM1, TNNT2, BMP4, MEF2C, PKP2, MYL2, NRG1	6.69
27	positive regulation of cardiocyte differentiation	Biological process	5/376	41/20400	0.00040	0.0097	BMP4, NRG1, EDN1, MEF2C, GPER1	6.62
28	mammary gland duct morphogenesis	Biological process	4/376	33/20400	0.0012	0.020	AREG, ETV5, CAV3, DDR1	6.58
29	regulation of cardiac muscle cell differentiation	Biological process	6/376	50/20400	0.00015	0.0052	BMP4, NRG1, CAV3, DKK1, EDN1, MEF2C	6.51
30	myoblast differentiation	Biological process	10/376	84/20400	2.6E-06	0.00031	IL18, BMP4, PLEKHM3, JAG1, PRICKLE1, RBM24, ANKRD2, NRG1, IGFBP3, MEF2C	6.46

GeneRatio: Number of differentially expressed genes of a GO term / Total number of differentially expressed genes

BgRatio: Number of genes of a GO term / Total number of genes in GO database for the corresponding species

Enrichment factor: GeneRatio/BgRatio

Table S8. Top 30 of KEGG pathway enrichment of differentially expressed genes of HeLa cells on the micropillar array

No.	Pathway	TYPE	GeneRatio	BgRatio	p value	q value	Genes	Enrichment factor
1	Vitamin B6 metabolism	<i>Metabolism: Metabolism of cofactors and vitamins</i>	1/160	6/7528	0.015	0.18	AOX1	7.84
2	Histidine metabolism	<i>Metabolism: Amino acid metabolism</i>	3/160	23/7528	0.0034	0.13	ALDH3A1, HDC, ALDH7A1	6.14
3	Riboflavin metabolism	<i>Metabolism: Metabolism of cofactors and vitamins</i>	1/160	8/7528	0.026	0.22	ENPP1	5.88
4	Staphylococcus aureus infection	<i>Human Diseases: Infectious disease: bacterial</i>	8/160	68/7528	5.1E-05	0.012	C1R, FCGR2C, HLA-DRB5, CFB, ICAM1, C5, C3, FCGR2A	5.54
5	African trypanosomiasis	<i>Human Diseases: Infectious disease: parasitic</i>	4/160	37/7528	0.0028	0.13	IL18, ICAM1, PLCB4, IL6	5.09
6	Malaria	<i>Human Diseases: Infectious disease: parasitic</i>	5/160	49/7528	0.0016	0.093	IL18, CD36, ICAM1, SDC2, IL6	4.8
7	Nicotinate and nicotinamide metabolism	<i>Metabolism: Metabolism of cofactors and vitamins</i>	3/160	30/7528	0.0087	0.20	AOX1, ENPP1, NT5E	4.71
8	Other types of O-glycan biosynthesis	<i>Metabolism: Glycan biosynthesis and metabolism</i>	2/160	22/7528	0.025	0.24	LFNG, ST6GAL1	4.28
9	Apoptosis - multiple species	<i>Cellular Processes: Cell growth and death</i>	3/160	33/7528	0.012	0.22	BCL2L11, BCL2L1, BBC3	4.28

10	Prion diseases	<i>Human Diseases:</i> Neurodegenerative disease	3/160	35/7528	0.015	0.20	EGR1, C5, IL6	4.03
11	Starch and sucrose metabolism	<i>Metabolism:</i> Carbohydrate metabolism	3/160	36/7528	0.016	0.19	ENPP1, GAA, AMY1C	3.92
12	Tyrosine metabolism	<i>Metabolism:</i> Amino acid metabolism	3/160	36/7528	0.016	0.19	AOX1, ALDH3A1, TYRP1	3.92
13	Glycosaminoglycan biosynthesis - heparan sulfate / heparin	<i>Metabolism:</i> Glycan biosynthesis and metabolism	2/160	24/7528	0.031	0.24	HS3ST3B1, B3GAT3	3.92
14	Hypertrophic cardiomyopathy (HCM)	<i>Human Diseases:</i> Cardiovascular disease	7/160	85/7528	0.0013	0.10	MYL2, ITGA11, TNNC1, IL6, TPM1, TNNT2, EDN1	3.87
15	Complement and coagulation cascades	<i>Organismal Systems:</i> Immune system	6/160	79/7528	0.0039	0.13	C1R, CFB, F3, C5, C4BPA, C3	3.57
16	Bladder cancer	<i>Human Diseases:</i> Cancer: specific types	3/160	41/7528	0.025	0.23	HBEGF, DAPK2, RPS6KA5	3.44
17	Fluid shear stress and atherosclerosis	<i>Human Diseases:</i> Cardiovascular disease	10/160	139/7528	0.00065	0.075	DUSP1, MEF2C, CAV1, CAV2, BMP4, CAV3, GSTM2, ICAM1, SDC2, EDN1	3.38
18	PPAR signaling pathway	<i>Organismal Systems:</i> Endocrine system	5/160	74/7528	0.012	0.23	ANGPTL4, ACADL, OLR1, CD36, FABP7	3.18
19	Pertussis	<i>Human Diseases:</i> Infectious disease: bacterial	5/160	76/7528	0.014	0.23	C1R, C5, C4BPA, IL6, C3	3.1
20	Rheumatoid	<i>Human</i>	6/160	91/7528	0.0084	0.22	IL18,	3.1

	arthritis	<i>Diseases:</i> Immune disease					HLA-DRB5, ANGPT1, ICAM1, ATP6V0A4, IL6	
21	Basal cell carcinoma	<i>Human Diseases:</i> Cancer: specific types	4/160	63/7528	0.025	0.23	WNT7B, HHIP, BMP4, FZD10	2.99
22	AGE-RAGE signaling pathway in diabetic complications	<i>Human Diseases:</i> Endocrine and metabolic disease	6/160	100/7528	0.014	0.21	EGR1, F3, ICAM1, PLCB4, IL6, EDN1	2.82
23	Apelin signaling pathway	<i>Environment and Information Processing:</i> Signal transduction	8/160	137/7528	0.0072	0.21	EGR1, MEF2C, CTGF, MYL2, MYLK, JAG1, PLCB4, ACTA2	2.75
24	Dilated cardiomyopathy (DCM)	<i>Human Diseases:</i> Cardiovascular disease	5/160	91/7528	0.031	0.24	MYL2, ITGA11, TNNC1, TPM1, TNNT2	2.59
25	Leishmaniasis	<i>Human Diseases:</i> Infectious disease: parasitic	4/160	74/7528	0.047	0.32	FCGR2C, HLA-DRB5, C3, FCGR2A	2.54
26	Vascular smooth muscle contraction	<i>Organismal Systems:</i> Circulatory system	7/160	132/7528	0.018	0.18	MYLK, MYL9, ACTG2, ADM, PLCB4, EDN1, ACTA2	2.5
27	Phagosome	<i>Cellular Processes:</i> Transport and catabolism	8/160	152/7528	0.014	0.20	C1R, FCGR2C, HLA-DRB5, OLR1, CD36, ATP6V0A4, C3, FCGR2A	2.48
28	Hippo signaling pathway	<i>Environment and Information Processing:</i> Signal transduction	8/160	154/7528	0.015	0.19	CRB1, WNT7B, CTGF, BMP4, AREG, BBC3, AJUBA, FZD10	2.44
29	Wnt signaling pathway	<i>Environment and Information Processing:</i>	8/160	158/7528	0.017	0.18	DKK1, WNT7B, ROR1, CXXC4,	2.38

		Signal transduction				PRICKLE1, PLCB4, CTNNBIP1, FZD10		
30	Proteoglycans in cancer	<i>Human Diseases: Cancer: overview</i>	10/160	201/7528	0.011	0.23	HSPB2, HBEGF, WNT7B, CAV1, CAV2, CAV3, RDX, SDC2, FLNA, FZD10	2.34

Gene Ratio: Number of differentially expressed genes of a KEGG term / Total number of differentially expressed genes

Bg Ratio: Number of genes of a KEGG term / Total number of genes in KEGG database for the corresponding species

Enrichment factor: GeneRatio/BgRatio

Note:

The criterion of enriching the GO terms and KEGG pathways is *p* value lower than 0.05 by Fisher's exact probability test. The *p* value is a measure of probability of this compound data if no real difference exists. Therefore, a small *p* value indicates a small chance of getting this data if no real difference exists and thus higher probability of a significant difference between two groups.

During multiple testing, false positives might be produced by chance with a *p*-value threshold. A *q*-value, that is a False Discovery Rate (FDR) adjusted *p*-value, was used in the enrichment of GO and KEGG pathway to overcoming the problem. The *q*-value gives a far more accurate indication of the level of false positives for a given cut-off value.

While all of the terms in Tables S7 and S8 exhibited *p* < 0.05, the behaviors of the *q* values are quite different: 29 of the 30 KEGG terms in Table S8 led to *q* > 0.05, and all of the 30 GO terms in Table S8 led to *q* < 0.05. So, these 30 GO terms seem more important to reflect the key difference of gene expression of HeLa cells on the micropillar array compared with on the smooth surface.

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