**Supplementary Information**

Note: the full legend description is located in the last page when several pages are necessary for a figure/table.

Supplementary Table 1. Results of proteomics data including phosphoproteomics and cytokine level measurements for NHBE and NRBE cells exposed to 52 stimuli.

The file contains the median of bead fluorescence intensities measured for each protein in every sample (cell lysate and corresponding supernatant for phosphoproteins and cytokines, respectively). For each stimulus, sample replicates have been extracted from 3 independent wells. The results are reported for (a) 19 phosphoproteins, with in addition the measurements for 2 control beads (Control A: Phycoerythrin-coated beads used as positive control bead; Control B: BSA-coated beads devoid of antibody used as negative control bead), and for the actin; (b) 22 cytokines.

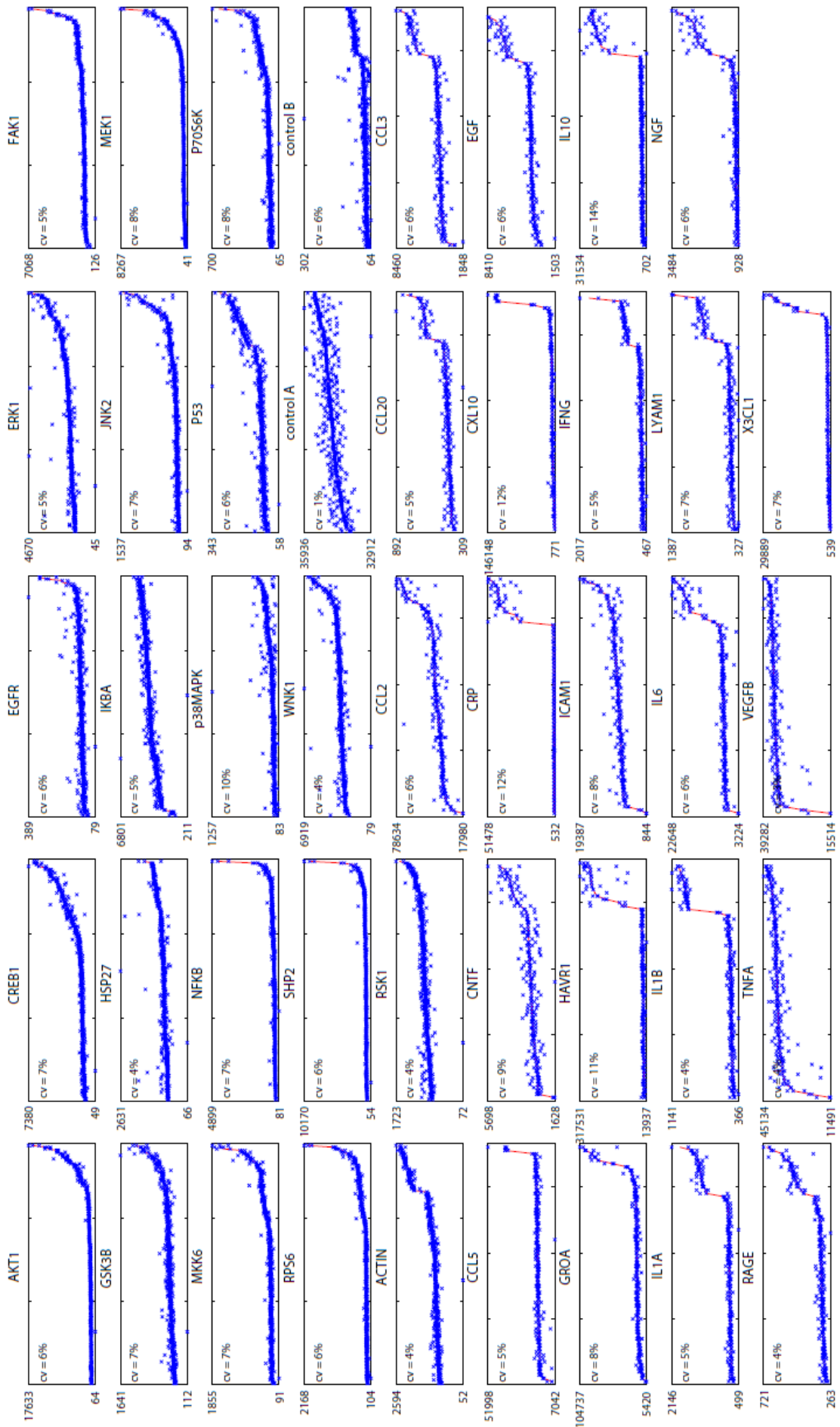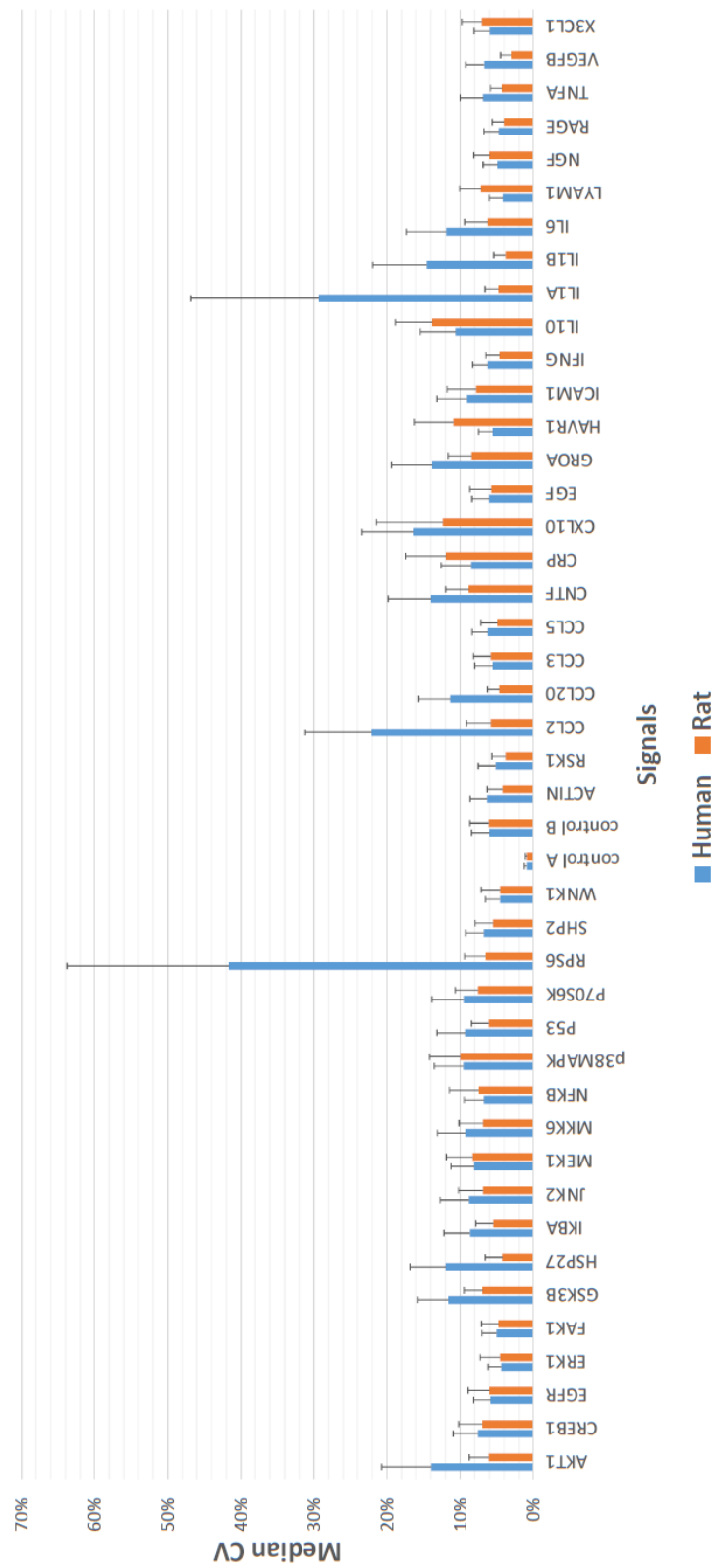The data are accessible in Figshare: http://dx.doi.org/10.6084/m9.figshare.960097
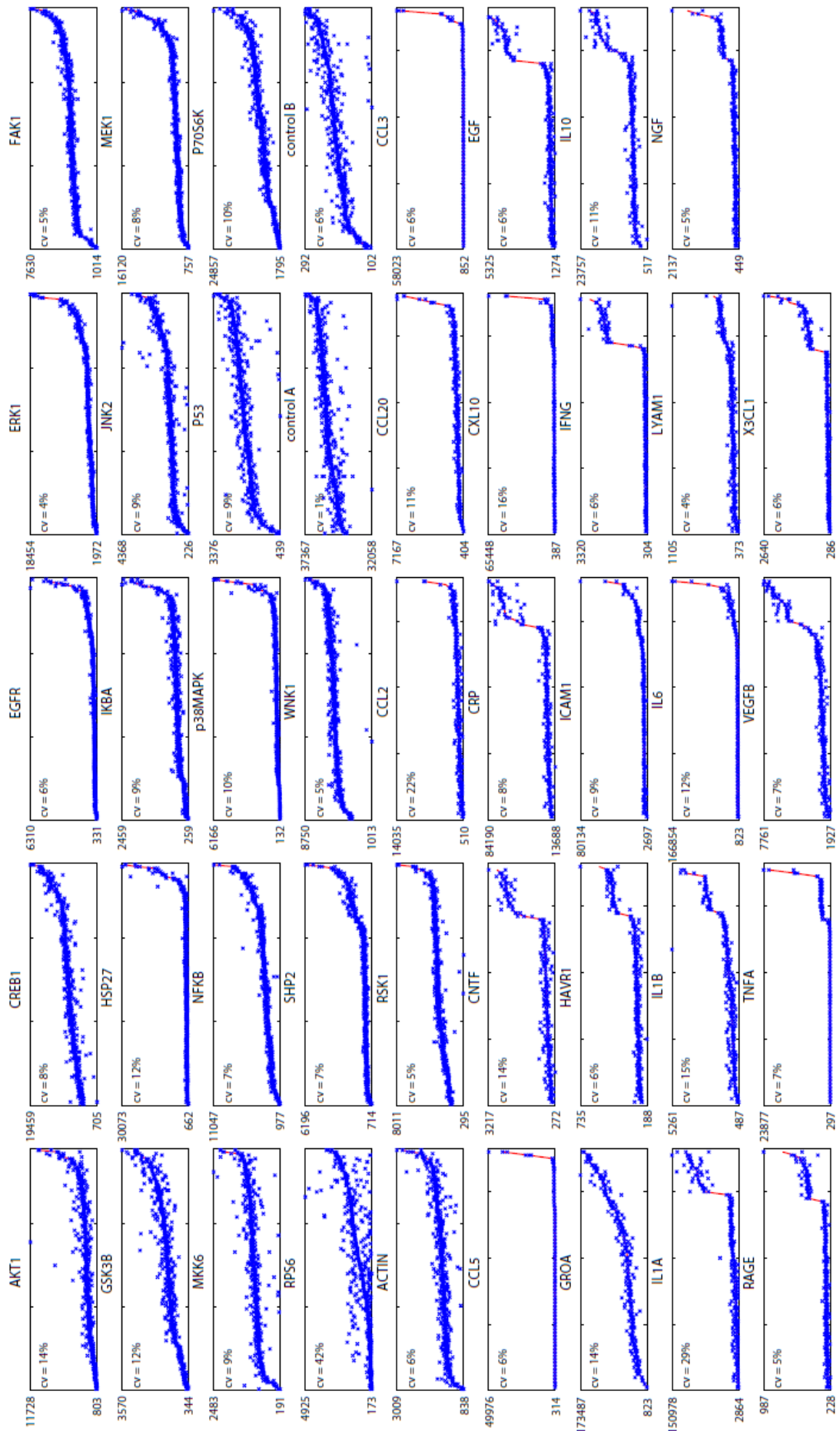
Supplementary Figure 1. Quality assessment of proteomics data (to be continued).

Supplementary Figure 1. Quality assessment of proteomics data (to be continued).

4

C

Supplementary Figure 1. Quality assessment of proteomics data.

Panel A and B: Raw data (fluorescent intensity) of each protein (indicated in the subplot title) for human (A) and rat (B) cells. On the x-axis data are sorted by raw median value of the triplicates across all conditions. For each protein (subplot) the y-axis ranges from minimum FI to maximum FI across all conditions. Each data point is represented by an 'x' lying above or below the red line that represents the median value of each set of replicates. The median of all the coefficients of variation of the replicate measurements is reported in the upper left corner of each plot. Panel C: Median CVs across all conditions for human (blue bars) and rat (orange bars) data together with the median absolute deviation from the median (MAD).

Supplementary Table 2. Results of phosphoprotein measurements in NHBE and NRBE using antibody-bead based assays for the experimental screening of 270 stimuli.

After an exposure of 5 minutes to each stimulus, cells were lysed and used to measure phosphoproteins. Data were analyzed and a final selection of 52 stimuli used for the main experiment was performed (Data deposited in the figshare public repository).

The data are accessible in Figshare: http://dx.doi.org/10.6084/m9.figshare.960097
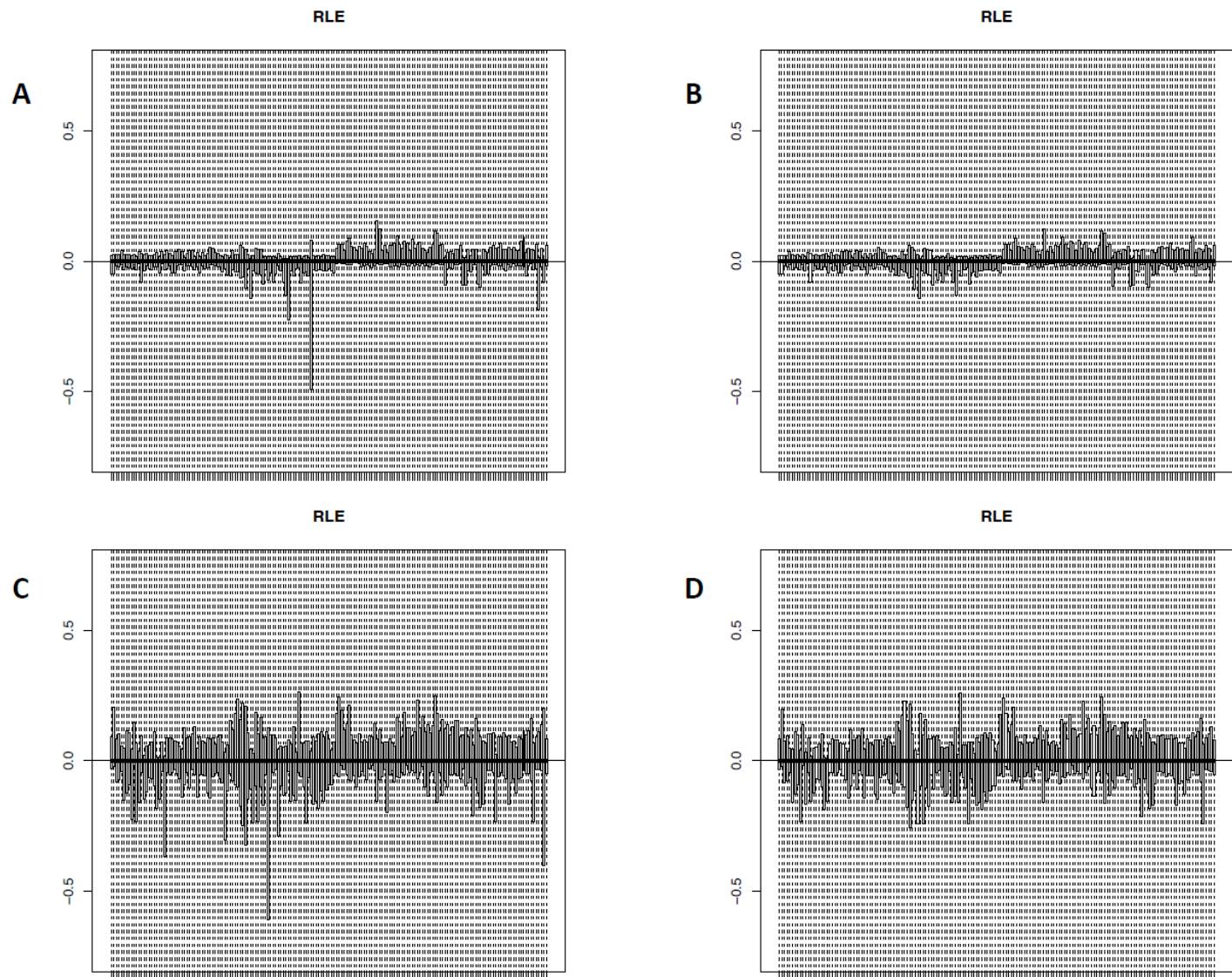
Supplementary Figure 2. Quality assessment of gene expression data (to be continued).

E

NUSE

F

NUSE

G

NUSE

H

NUSE
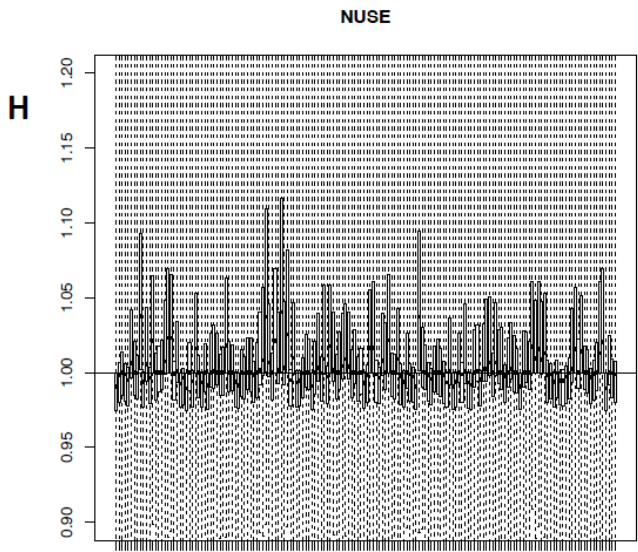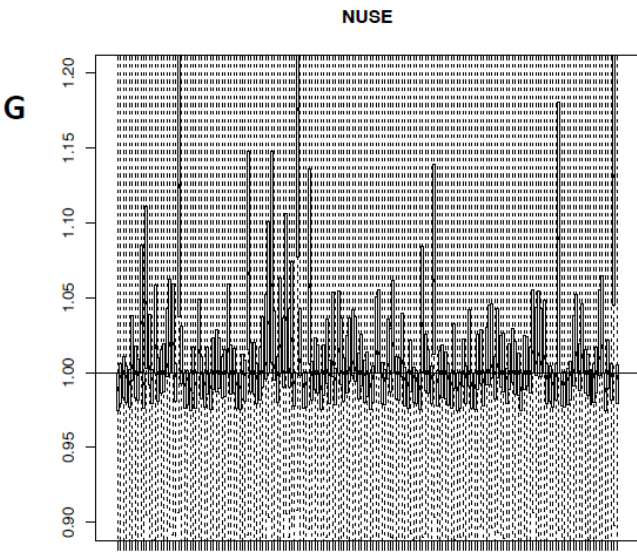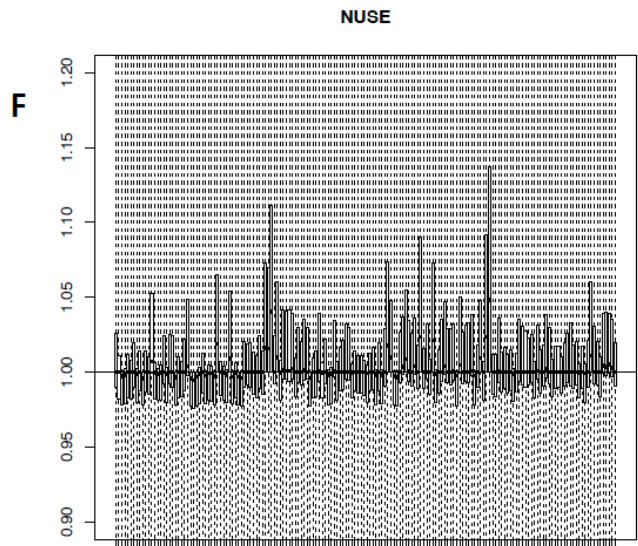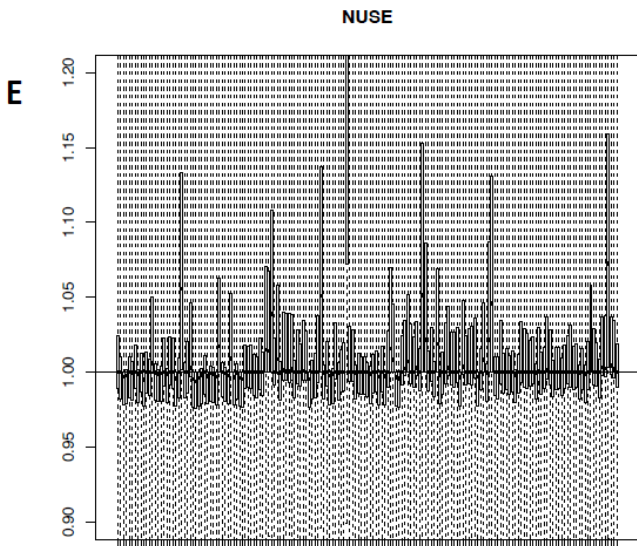
Supplementary Figure 2. Quality assessment of gene expression data (to be continued).
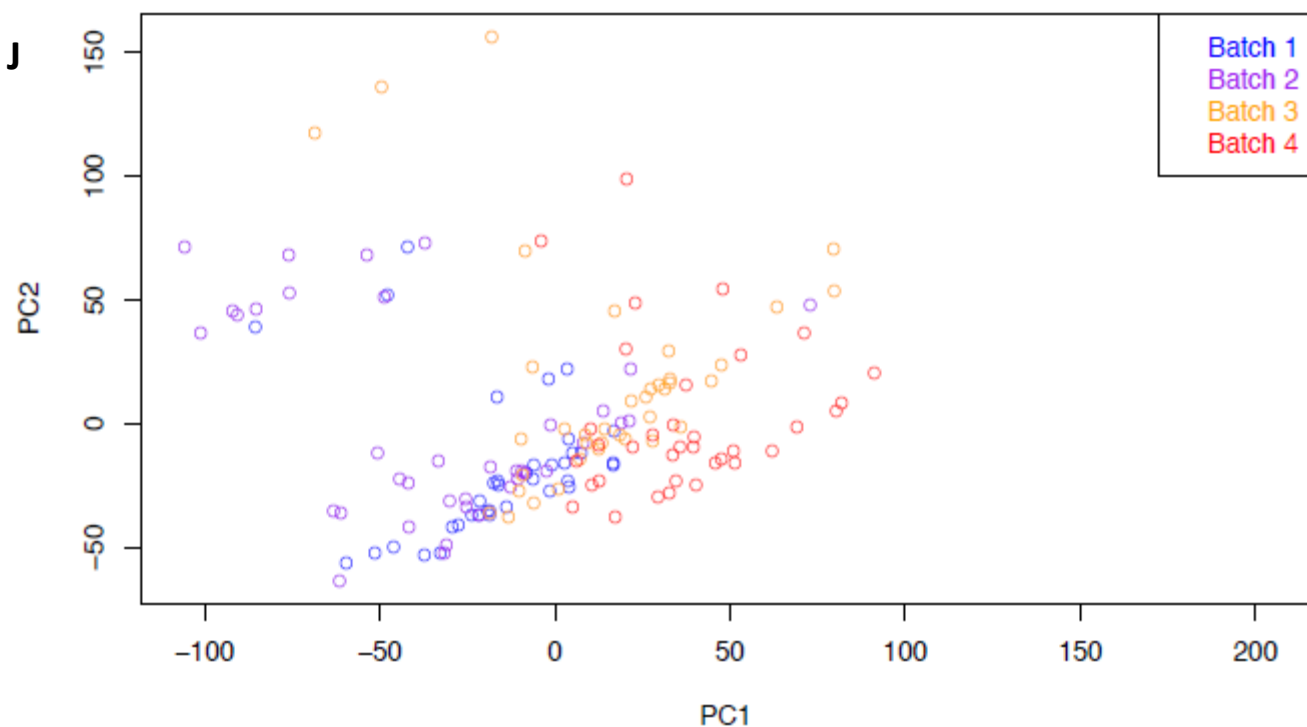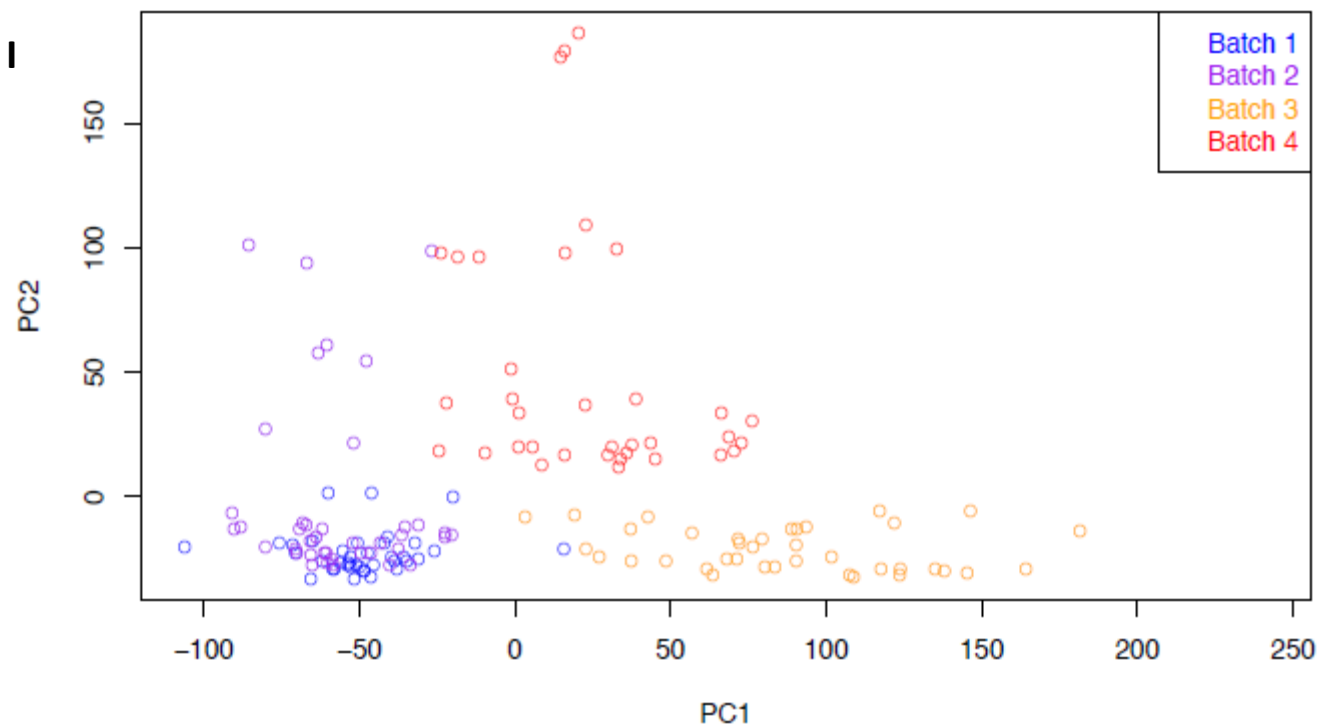
Supplementary Figure 2. Quality assessment of gene expression data.

Relative log expression (RLE, A and B for human, C and D for rat) and normalized unscaled standard error (NUSE, E and F for human, G and H for rat) boxplots were generated before (A, C, E, G) and after (B, D, F, H) the exclusion of low quality chips. When CEL files were excluded, the remaining data were re-processed together using GCRMA. Principal component analysis of centered and non-scaled GCRMA-normalized human and rat gene expression data was conducted. Individual samples are colored by their respective batch. (I) The first two principal components for human gene expression data each explain 29.5% and 15.0% of the total variance. (J) The first two principal components for rat gene expression data each explain 17.1% and 13.8% of the total variance.
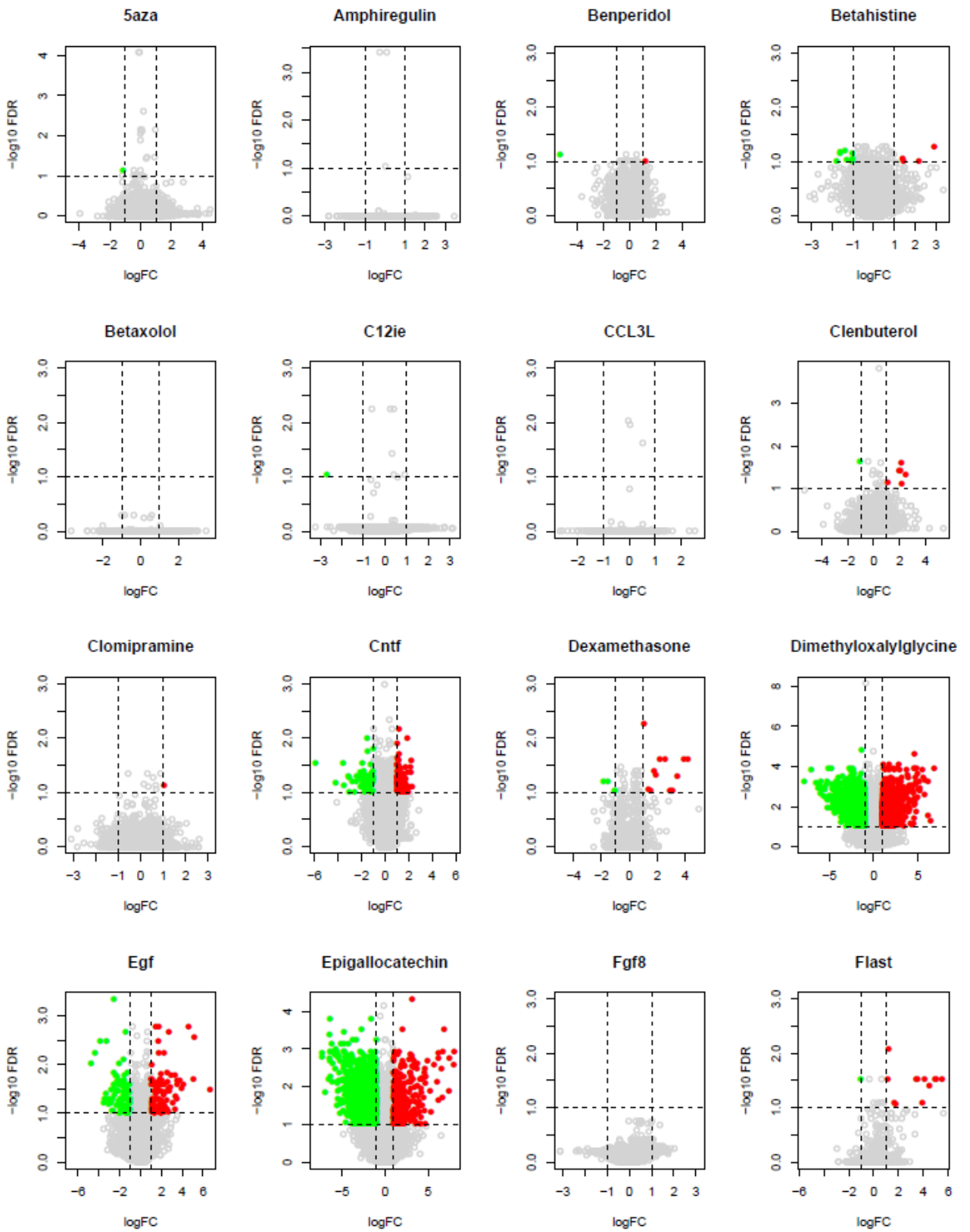
Supplementary Figure 3. Differential gene expression analysis of NHBE data (to be continued).
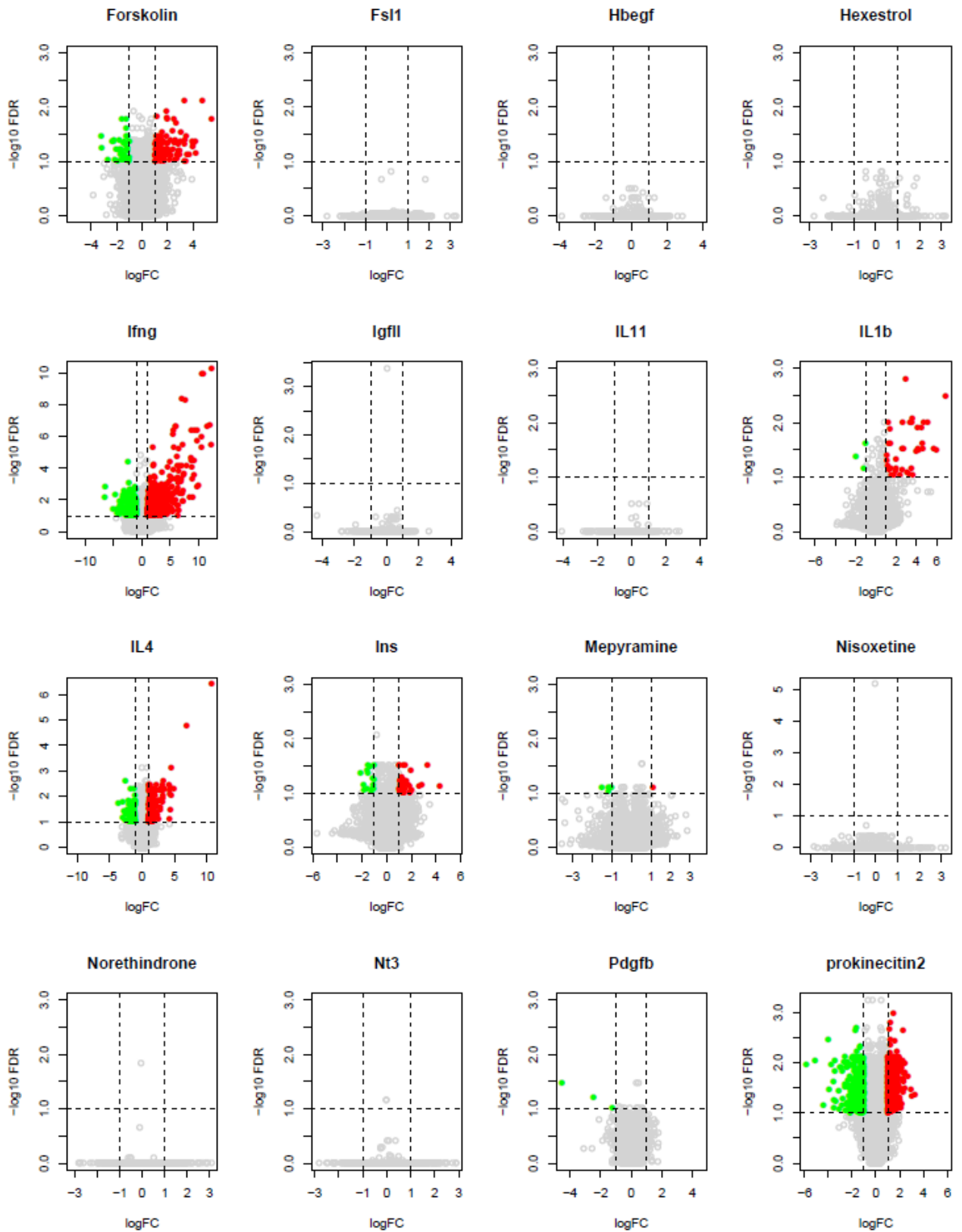
Supplementary Figure 3. Differential gene expression analysis of NHBE data (to be continued).
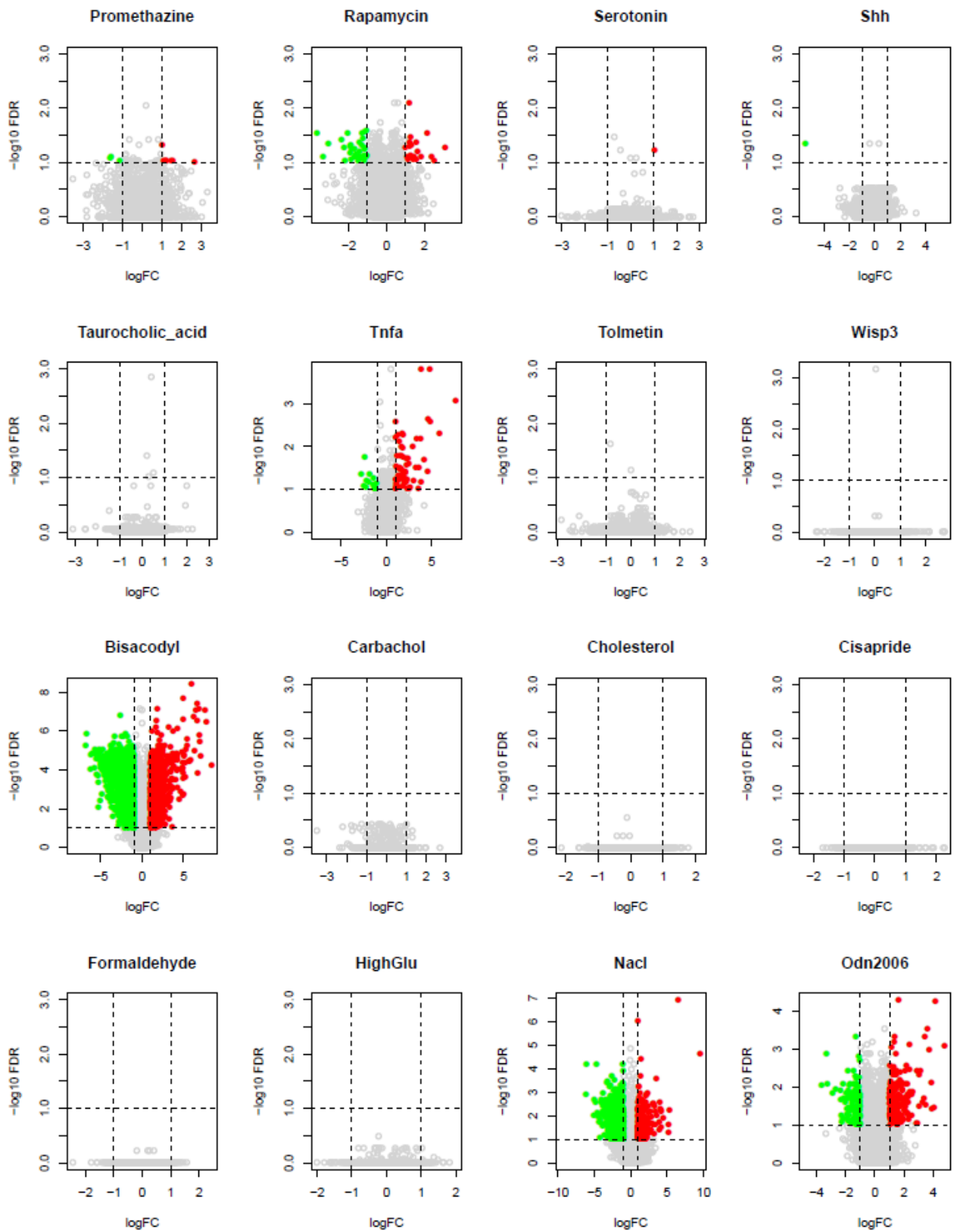
Supplementary Figure 3. Differential gene expression analysis of NHBE data (to be continued).

Supplementary Figure 3. Differential gene expression analysis of NHBE data.

Each subplot represents a volcano plot for each stimulus. The x-axis represents the differential expression between DME control vs individual stimulus treatment expressed as log base 2 fold change (logFC). The y-axis represents the significance level of the differential expression expressed as -log base 10 false discovery rate (-log10FDR). The vertical dotted lines illustrate differential expression of -1 and +1 as log FC, and the horizontal line represents a FDR threshold of 0.1. Dots beyond these lines are colored in green (down-regulation) or in red (up-regulatino), and represent genes that have associated logFC and FDR values beyond these dotted lines.

Supplementary Figure 4. Differential gene expression analysis of NRBE data (to be continued).
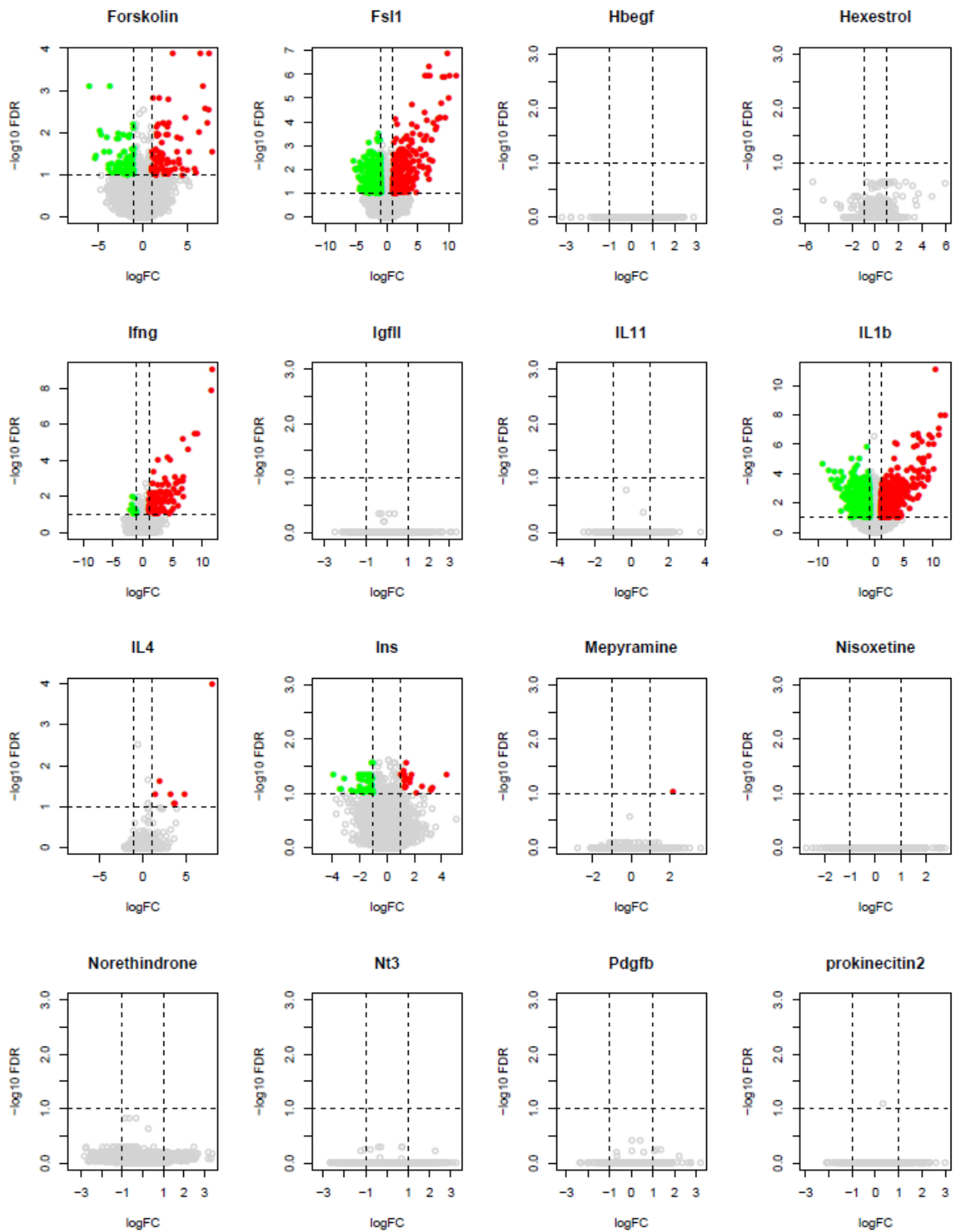
Supplementary Figure 4. Differential gene expression analysis of NRBE data (to be continued).
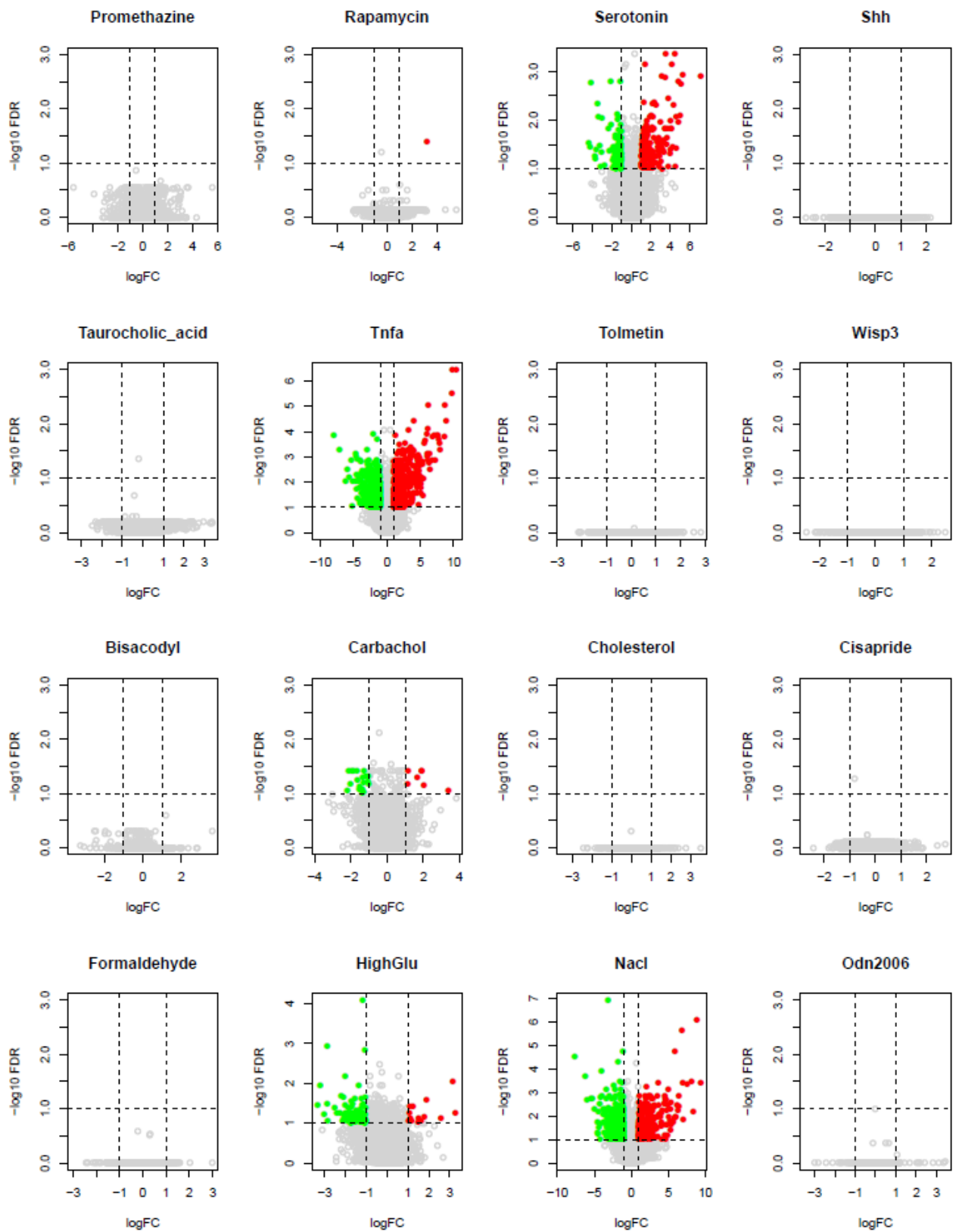
Supplementary Figure 4. Differential gene expression analysis of NRBE data (to be continued).
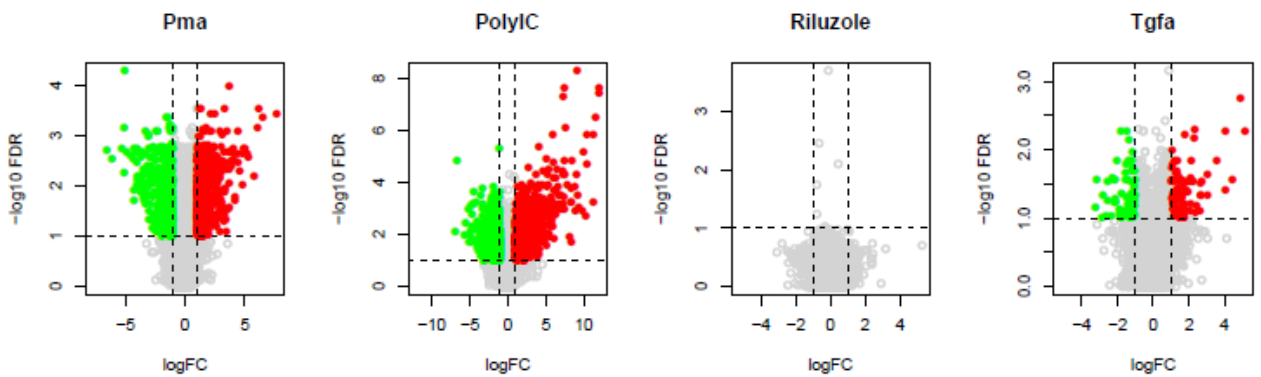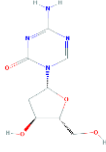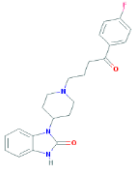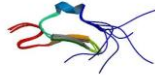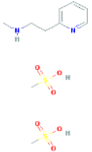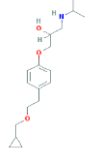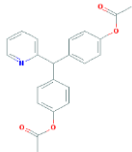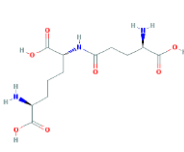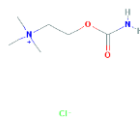
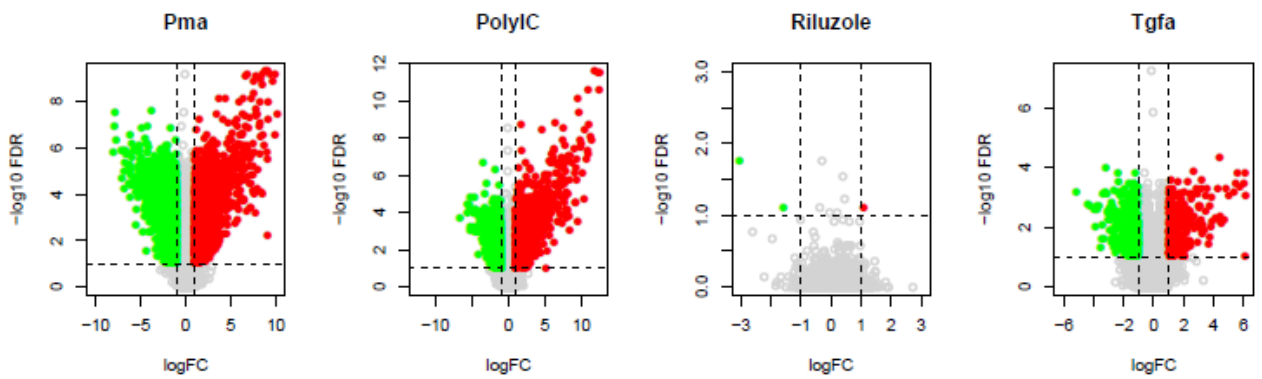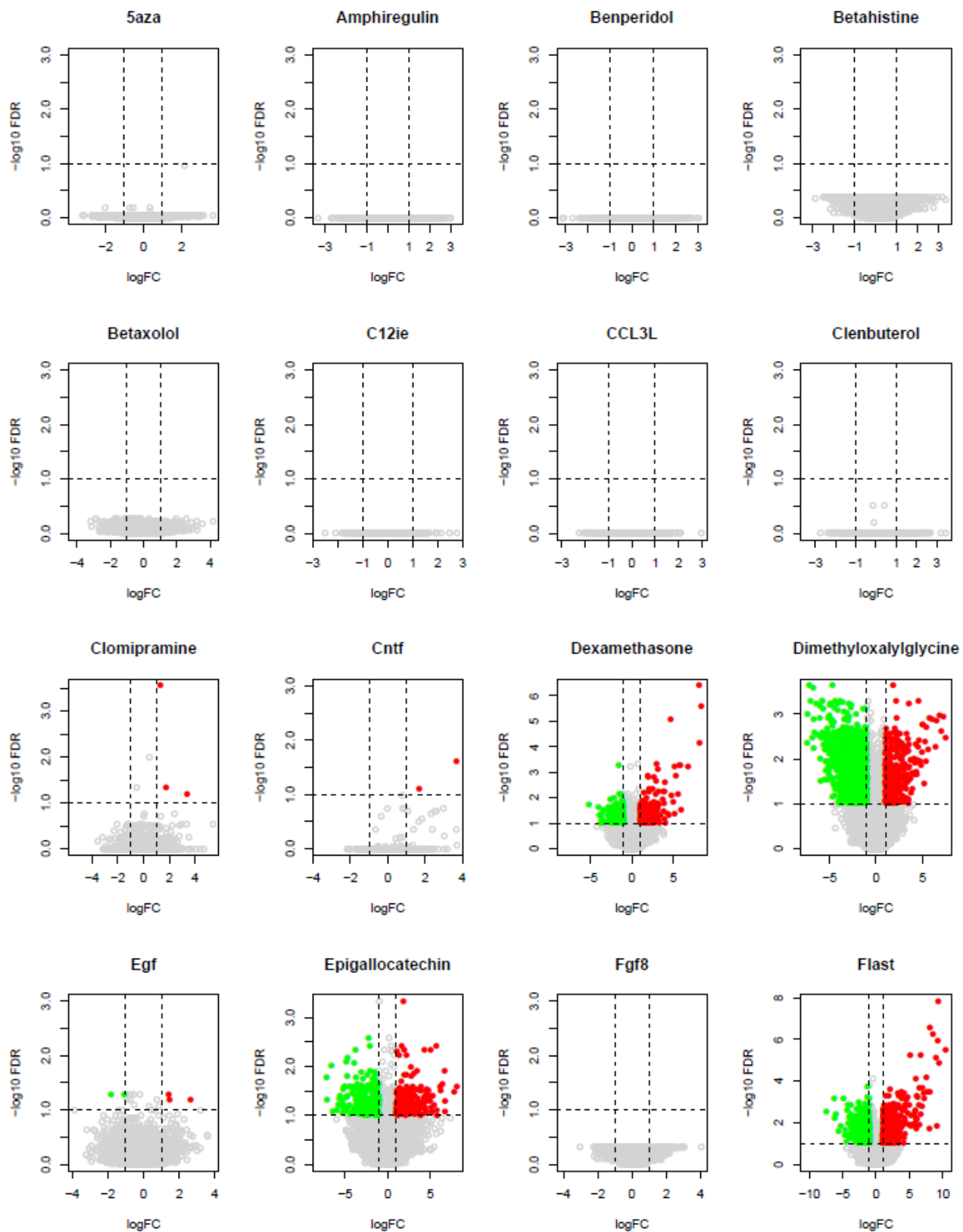Supplementary Figure 4. Differential gene expression analysis of NRBE data.

Each subplot represents a volcano plot for each stimulus. The x-axis represents the differential expression between DME control vs individual stimulus treatment expressed as log base 2 fold change (logFC). The y-axis represents the significance level of the differential expression expressed as –log base 10 false discovery rate (-log10FDR). The vertical dotted lines illustrate differential expression of -1 and +1 as log FC, and the horizontal line represents a FDR threshold of 0.1. Dots beyond these lines are colored in green (down-regulation) or in red (up-regulatino), and represent genes that have associated logFC and FDR values beyond these dotted lines.

|	PROTEIN NAME	HUMAN PLEX	RAT PLEX
PHOSPHOPROTEINS	AKT1	BioRad: 171-V50001M	PRT: P-AKT1-A01
	CREB1	PRT: P-CREB1-A01	PRT: P-CREB1-A01
	EGFR	PRT: P-EGFR-A01	PRT: P-EGFR-A01
	ERK1	PRT: P-MK03-A01	PRT: P-MK03-A01
	FAK1	RnD: DYC4528	RnD: DYC4528
	GSK3B	BioRad: 171-V50007M	RnD: DYC1590
	HSP27	PRT: P-HSPB1-A01	PRT: P-HSPB1-A01
	IKBA	PRT: P-IKBA-A01	PRT: P-IKBA-A01
	JNK2	RnD: DYC2236	RnD: DYC2236
	MEK1	PRT: P-MP2K1-A01	PRT: P-MP2K1-A01
	MKK6	RnD: DYC5586	RnD: DYC5586
	NFKB	PRT: P-NFKB-A01	PRT: P-NFKB-A01
	p38MAPK	BioRad: 171-V50014M	PRT: P-MK1234-A01
	P53	PRT: P-P53-A01	PRT: P-P53-A01
	P70S6K	BioRad: 171-V50015M	RnD: DYC8965, DYC896
	RPS6	RnD: DYC3918	RnD: DYC3918
	SHP2	RnD: DYC3790	RnD: DYC3790
	WNK1	RnD: DYC4720	RnD: DYC4720
	RSK1	RnD: DYC892	RnD: DYC892
	control A	PRT (custom order)	PRT (custom order)
	control B	PRT (custom order)	PRT (custom order)
	ACTIN	CST: 4970 and 5057	CST: 4970 and 5057
CYTOKINES	CCL2	PRT: CH-CCL2-A02	PRT: CR-CCL2-A02
	CCL20	RnD: DY360	RnD: DY540
	CCL3	PRT: CH-CCL3-A02	PRT: CR-CCL3-A02
	CCL5	PRT: CH-CCL5-A02	PRT: CR-CCL5-A02
	CNTF	PRT: CH-CNTF-A02	PRT: CR-CNTF-A02
	CRP	RnD: DY1707	RnD: DY1744
	CXL10	PRT: CH-CXL10-A02	PRT: CR-CXL10-A02
	EGF	PRT: CH-EGF-A02	PRT: CR-EGF-A02
	GROA	PRT: CH-GROA-A02	PRT: CR-GROA-A02
	HAVR1	RnD: DY1750	RnD: DY3689
	ICAM1	PRT: CH-ICAM1-A02	RnD: DY583
	IFNG	PRT: CH-IFNG-A02	PRT: CR-IFNG-A02
	IL10	PRT: CH-IL10-A02	RnD: DY522
	IL1A	PRT: CH-IL1A-A02	PRT: CR-IL1A-A02
	IL1B	RnD: DY201	RnD: DY201
	IL6	PRT: CH-IL6-A02	PRT: CR-IL6-A02
	LYAM1	RnD: DY728	RnD: DY1534
	NGAL	N/A	RnD: DY3508
	NGF	RnD: DY556	RnD: DY556
	RAGE	RnD: DY1616	RnD: DY1616
	TNFA	PRT: CH-TNFA-A02	PRT: CR-TNFA-A02
	VEGFB	PRT: CH-VEGFB-A02	PRT: CR-VEGFB-A02
	X3CL1	RnD: DY537	RnD: DY537
	Coupling Kit	Luminex: Cat#40-50016	
	Phopshoprotein preparation buffers	ProtATonce: Cat#PPK40-A01	
	Cytokine preparation assay buffers	ProtATonce: Cat#CTP40-A01	
	Multiplex measurement service	ProtATonce: Custom order	
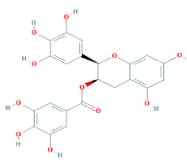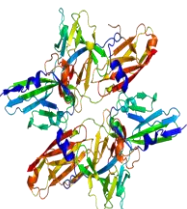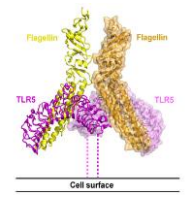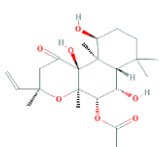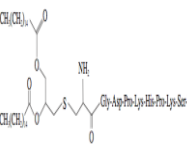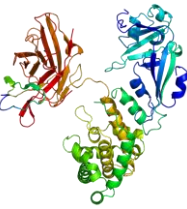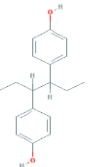
Supplementary Table 3. Catalogue numbers of antibody pairs used for multiplex bead assays.
RnD: RnD Systems, http://www.rndsystems.com/; CST: Cell Signaling Technology, http://www.cellsignal.com/;
BioRad: Bio-Rad Laboratories, http://www.bio-rad.com; PRT: ProtATonce ltd, http://www.protATonce.com
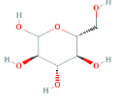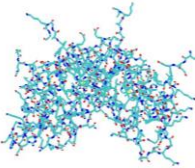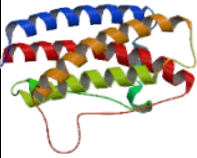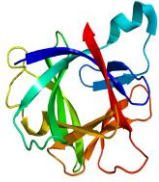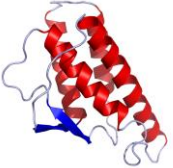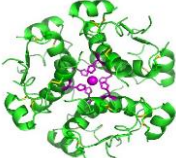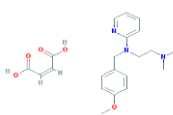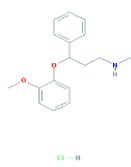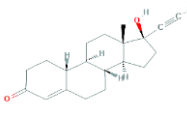
LEGEND	Supplier / Catalog # / CAS #	compound name from UniProt, PubChem or other source	compound ID from UniProt or PubChem	compound IMAGE from PubChem, PDB or other source	target concentration we used in ng/ml				Compound Function, Pharmacological Action or general Biological Effect. Sources: UniProt, PubChem, MeSH, other
					active IC50s	total IC50s	active screens	total screens	
					Supplier's name for compound				
1	SantaCruz / sc-202424 / 2353-33-5	decitabine	451668		1141				Antimetabolites/Antineoplastic, Enzyme Inhibitors, Teratogens, Methyltransferase Inhibitor
					6	17	6	308	
					5-Aza-2′-Deoxycytidine				
2	Prestwick / Prestw-484 / 2062-84-2	benperidol	16363		100				Antipsychotic Agents, Dopamine Antagonists
					0	12	4	289	
					Benperidol				
3	PeproTech / 100-55B / -	AREG (amphiregulin)	P15514		3967				Ligand of the EGF receptor/EGFR. Autocrine growth factor as well as a mitogen for a broad range of target cells including astrocytes, Schwann cells and fibroblasts
					-	-	-	-	
					Recombinant Human Amphiregulin				
4	Prestwick / Prestw-543 / 54856-23-4	betahistine	198334		5648				Histamine Agonists, Vasodilator Agents
					0	0	0	0	
					Betahistine mesylate				
5	Prestwick / Prestw-382 / 63659-19-8	betaxolol	107952		3989				Adrenergic beta-1 Receptor Antagonists, Antihypertensive Agents, Sympatholytics
					3	67	4	667	
					Betaxolol hydrochloride				
6	Prestwick / Prestw-419 / 603-50-9	bisacodyl	2391		3975				Cathartics
					4	158	11	550	
					Bisacodyl				
7	InvivoGen / tlrl-c12dap / -	C12-iE-DAP	45480617		1000				PGN-like molecule - recognized by the intracellular sensor NOD1, which results in NF-κB activation and the production of inflammatory cytokines
					-	-	-	-	
					C12-iE-DAP				
8	Prestwick / Prestw-880 / 51-83-2	carbachol	5831		3982				Analgesics, Non-Narcotic, Cardiotonic Agents, Cholinergic Agonists, Miotics
					41	178	11	295	
					Carbachol				
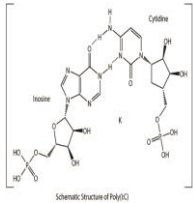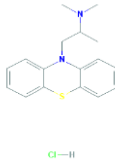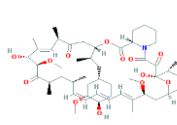
Supplementary Table 4. Final selection of 52 stimuli used in the main experiment (to be continued).

| | Supplier / Catalog # / CAS # | compound name from UniProt, PubChem or other source | compound ID from UniProt or PubChem | compound IMAGE from PubChem, PDB or other source | target concentration we used in ng/ml | | | | Compound Function, Pharmacological Action or general Biological Effect. Sources: UniProt, PubChem, MeSH, other |
| | | | | | active IC50s | total IC50s | active screens | total screens | |
					Supplier's name for compound				
9	PeproTech / 300-56 / -	CL3L1 (C-C motif chemokine 3-like 1)	P16619		200				Chemotactic for lymphocytes and monocytes. Is a ligand for CCR1, CCR3 and CCR5. Is an inhibitor of HIV-1-infection. The processed form LD78-beta(3-70) shows a 20-fold to 30-fold higher chemotactic activity
					-	-	-	-	
					Recombinant Human LD78β (CCL3L1)				
10	Sigma / C3045 / 57-88-5	cholesterol	5997		2000				Pharmaceutic aid (emulsifying agent). Cholesterol is used in liposomes to encapsulate and deliver chemotherapeutic drugs to diseased tissues. Cholesterol-C14 is used clinically as an organ imaging agent. Organs visualized by the technique include ovaries, adrenals, and spleen
					0	16	0	6	
					Cholesterol				
11	Prestwick / Prestw-430 / 81098-60-4	cisapride	2769		4007				Anti-Ulcer Agents, Gastrointestinal Agents, Serotonin Receptor Agonists
					55	155	0	4	
					Cisapride				
12	Prestwick / Prestw-345 / 21898-19-1	clenbuterol	5702273		4015				Adrenergic beta-Agonists, Bronchodilator Agents, Sympathomimetics
					2	39	7	457	
					Clenbuterol hydrochloride				
13	Prestwick / Prestw-269 / 17321-77-6	clomipramine	68539		4005				Antidepressive Agents: Tricyclic, Serotonin Uptake Inhibitors
					10	49	27	572	
					Clomipramine hydrochloride				
14	PeproTech / 450-13 // 450-50 / -	CNTF (ciliary neurotrophic factor)	P26441// P20294		200				CNTF is a survival factor for various neuronal cell types. Seems to prevent the degeneration of motor axons after axotomy
					-	-	-	-	
					Recombinant Human//Rat CNTF				
15	Prestwick / Prestw-130 / 1177-87-3	dexamethasone acetate	236702		392				Anti-Inflammatory Agents
					0	41	3	559	
					Dexamethasone acetate				
16	VWR / CAYM71210-10 / 89464-63-1	oxalylglycine	560326		175140				Dimethyloxallyl glycine (DMOG) is a cell permeable, competitive inhibitor of HIF-alpha prolyl hydroxylase (HIF-PH) (biomol.de)
					0	0	0	3	
					DIMETHYLOXALLYL GLYCINE				
17	PeproTech / AF-100-15 // 400-25 / -	EGF (pro-epidermal growth factor)	P01133// P07522		100				EGF stimulates the growth of various epidermal and epithelial tissues in vivo and in vitro and of some fibroblasts in cell culture. Magnesiotropic hormone that stimulates magnesium reabsorption in the renal distal convoluted tubule via engagement of EGFR and activation of the magnesium channel TRPM6
					-	-	-	-	
					Recombinant Human//Rat EGF				

20

Supplementary Table 4. Final selection of 52 stimuli used in the main experiment (to be continued).
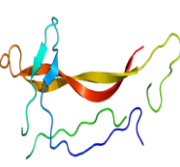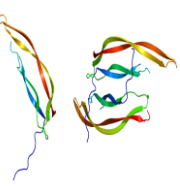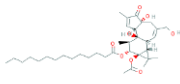
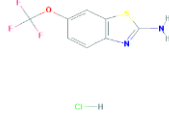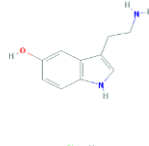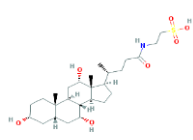| LEGEND	Supplier / Catalog # / CAS #	compound name from UniProt, PubChem or other source	compound ID from UniProt or PubChem	compound IMAGE from PubChem, PDB or other source	target concentration we used in ng/ml				Compound Function, Pharmacological Action or general Biological Effect. Sources: UniProt, PubChem, MeSH, other
					active IC50s	total IC50s	active screens	total screens	
					Supplier's name for compound				
18	SantaCruz / sc-200802 / 989-51-5	epigallocatechin gallate	65064		45840				Anticarcinogenic Agents, Antimutagenic Agents, Antioxidants, Neuroprotective Agents
					61	100	11	153	
					(-)-Epigallocatechin Gallate				
19	PeproTech / 100-25 / -	FGF8 (fibroblast growth factor 8)	P55075		100				Plays an important role in the regulation of embryonic development, cell proliferation, cell differentiation and cell migration. Required for normal brain, eye, ear and limb development during embryogenesis. Required for normal development of the gonadotropin-releasing hormone (GnRH) neuronal system
					-	-	-	-	
					Recombinant Human FGF-8				
20	InvivoGen / tlrl-pstfla / -	FLIC_SALTY (flagellin)	P06179		1000				Flagellin is the subunit protein which polymerizes to form the filaments of bacterial flagella. and is a proinflammatory molecule recognized by distinct types of pattern recognition receptors (PRRs): the surface localized Toll-like receptor (TLR5) and the cytosolic NOD-like receptors (NLRs), NLRC4 and NAIP5
					-	-	-	-	
					FLA-ST Ultrapure				
21	Sigma / 15512 / 50-00-0	formaldehyde	712		150				Disinfectants, Fixatives
					0	0	0	2	
					Formaldehyde solution				
22	SantaCruz / sc-3562 / 66575-29-9	forskolin	47936		4105				Potent activator of the adenylate cyclase system and the biosynthesis of cyclic AMP
					3	22	22	322	
					Forskolin				
23	InvivoGen / tlrl-fsl / -	FSL-1	-		1000				Synthetic diacylated lipoprotein - TLR2/TLR6 ligand
					-	-	-	-	
					FSL-1				
24	PeproTech / 100-47 / -	HBEGF (proheparin-binding EGF-like growth factor)	Q99075		50				Growth factor that mediates its effects via EGFR, ERBB2 and ERBB4. Required for normal cardiac valve formation and normal heart function. Promotes smooth muscle cell proliferation. May be involved in macrophage-mediated cellular proliferation. It is mitogenic for fibroblasts, but not endothelial cells. It is able to bind EGF receptor/EGFR with higher affinity than EGF itself and is a far more potent mitogen for smooth muscle cells than EGF. Also acts as a diphtheria toxin receptor
					-	-	-	-	
					Recombinant Human HB-EGF				
25	Prestwick / Prestw-699 / 84-16-2	hexestrol	3606		4001				Antineoplastic Agents, Hormonal, Estrogens/Non-Steroidal
					1	13	1	285	
					Hexestrol				

Supplementary Table 4. Final selection of 52 stimuli used in the main experiment (to be continued).
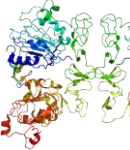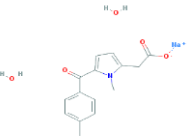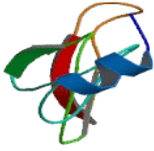
	Supplier / Catalog # / CAS #	compound name from UniProt, PubChem or other source	compound ID from UniProt or PubChem	compound IMAGE from PubChem, PDB or other source	target concentration we used in ng/ml				Compound Function, Pharmacological Action or general Biological Effect. Sources: UniProt, PubChem, MeSH, other
LEGEND					active IC50s	total IC50s	active screens	total screens	
					Supplier's name for compound				
26	SantaCruz / sc-211203 / 50-99-7	glucose	5793		9008000				Sweetening Agents
					0	4	0	5	
					D(+)Glucose, Anhydrous				
27	PeproTech / 300-02 // 400-20 / -	IFNG (interferon gamma)	P01579// P01581		100				Produced by lymphocytes activated by specific antigens or mitogens. IFN-gamma, in addition to having antiviral activity, has important immunoregulatory functions. It is a potent activator of macrophages, it has antiproliferative effects on transformed cells and it can potentiate the antiviral and antitumor effects of the type I interferons
					-	-	-	-	
					Recombinant Human//Rat IFN-γ				
28	PeproTech / 100-12 / -	IGF2 (insulin-like growth factor II)	P01344		100				The insulin-like growth factors possess mitogensgrowth-promoting activity, influenced by placental lactogen, IGF-II may play a role in fetal development. Preptin undergoes glucose-mediated co-secretion with insulin, and acts as physiological amplifier of glucose-mediated insulin secretion. Exhibits osteogenic properties by increasing osteoblast mitogenic activity through phosphoactivation of MAPK1 and MAPK3
					-	-	-	-	
					Recombinant Human IGF-II				
29	PeproTech / 200-11 / -	IL11 (interleukin-11)	P20809		100				Directly stimulates the proliferation of hematopoietic stem cells and megakaryocyte progenitor cells and induces megakaryocyte maturation resulting in increased platelet production.
					-	-	-	-	
					Recombinant Human IL-11				
30	PeproTech / 200-01B // 400-01B / -	IL1B (interleukin-1 beta)	P01584// Q63264		50				Produced by activated macrophages, IL-1 stimulates thymocyte proliferation by inducing IL-2 release, B-cell maturation and proliferation, and fibroblast growth factor activity. IL-1 proteins are involved in the inflammatory response, being identified as endogenous pyrogens, and are reported to stimulate the release of prostaglandin and collagenase from synovial cells
					-	-	-	-	
					Recombinant Huma//Rat IL-1β				
31	PeproTech / 200-04 // 400-04 / -	IL4 (interleukin-4)	P05112// P20096		100				Participates in at least several B-cell activation processes as well as of other cell types. It is a costimulator of DNA-synthesis. It induces the expression of class II MHC molecules on resting B-cells. It enhances both secretion and cell surface expression of IgE and IgG1. It also regulates the expression of the low affinity Fc receptor for IgE (CD23) on both lymphocytes and monocytes
					-	-	-	-	
					Recombinant Human//Rat IL-4				
32	Sigma / I9278 / 11061-68-0	INS (insulin)	P01308		1722				Insulin decreases blood glucose concentration. It increases cell permeability to monosaccharides, amino acids and fatty acids. It accelerates glycolysis, the pentose phosphate cycle, and glycogen synthesis in liver
					-	-	-	-	
					Insulin solution human				

Supplementary Table 4. Final selection of 52 stimuli used in the main experiment (to be continued).

LEGEND	Supplier / Catalog # / CAS #	compound name from UniProt, PubChem or other source	compound ID from UniProt or PubChem	compound IMAGE from PubChem, PDB or other source	target concentration we used in ng/ml				Compound Function, Pharmacological Action or general Biological Effect. Sources: UniProt, PubChem, MeSH, other
					active IC50s	total IC50s	active screens	total screens	
					Supplier's name for compound				
33	SantaCruz / sc-203629 / 59-33-6	pyrilamine	5284451		2854				Anti-Allergic Agents, Histamine H1 Antagonists
					3	53	3	805	
					Mepyramine maleate				
34	Sigma / S5886 / 7647-14-5	sodium chloride	5234	Cl------Na$^+$	8766000				Sodium Chloride (NaCl) is found in nature, in all body tissue, and is considered an essential nutrient (SantaCruz)
					0	0	0	0	
					Sodium Chloride				
35	Prestwick / Prestw-910 / 57754-86-6	nisoxetine	134453		3528				Nisoxetine hydrochloride is a selective and potent inhibitor of noradrenaline uptake with little or no affinity for a range of other neurotransmitter receptors. Nisoxetine hydrochloride is an inhibitor of SLC6A2 (SantaCruz)
					4	18	1	313	
					Nisoxetine hydrochloride				
36	Prestwick / Prestw-253 / 68-22-4	norethindrone	6230		3999				Contraceptives/ Oral/ Synthetic
					9	133	1	320	
					Norethindrone				
37	PeproTech / 450-03 / -	NTF3 (neurotrophin-3)	P20783		200				Seems to promote the survival of visceral and proprioceptive sensory neurons
					-	-	-	-	
					Recombinant Human NT-3				
38	InvivoGen / tlrl-2006 / -	ODN2006	-	InvivoGen Innovation within Reach	18259				Class B CpG oligonucleotide - Human TLR9 ligand
					-	-	-	-	
				5'-tcgtcgttttgtcgttttgtcgtt-3'	ODN 2006 (ODN 7909)				
39	PeproTech R&Dsystem / 100-14B // 520-BB-050 / -	PDGFB (platelet-derived growth factor subunit B)	P01127// Q05028		50				Growth factor that plays an essential role in the regulation of embryonic development, cell proliferation, cell migration, survival and chemotaxis. Potent mitogen for cells of mesenchymal origin. Required for normal blood vessel, skin, lung, heart, placenta, and kidney glomeruli development. Plays an important role in wound healing. Signaling is modulated by the formation of heterodimers with PDGFA
					-	-	-	-	
					Recombinant Human//Rat PDGF-BB				
40	Sigma / P1585 / 16561-29-8	tetradecanoylphorbol acetate	27924		500				PMA potent activator of protein Kinase C (PKC)
					8	8	2	26	
					Phorbol 12-myristate 13-acetate				

Supplementary Table 4. Final selection of 52 stimuli used in the main experiment (to be continued).

	Supplier / Catalog # / CAS #	compound name from UniProt, PubChem or other source	compound ID from UniProt or PubChem	compound IMAGE from PubChem, PDB or other source	target concentration we used in ng/ml — active IC50s	total IC50s	active screens	total screens	Compound Function, Pharmacological Action or general Biological Effect. Sources: UniProt, PubChem, MeSH, other
41	InvivoGen / tlrl-pic / 31852-29-6	Poly(I:C)	-	Schematic Structure of Poly(I:C)	**10000** —	-	-	-	Polyinosinic-polycytidylic acid (poly(I:C)) is a synthetic analog of double-stranded RNA (dsRNA), a molecular pattern associated with viral infection. Poly(I:C) is recognized by TLR3 inducing the activation of NF-kB and the production of cytokines
				Poly(I:C) High Molecular Weight					
42	PeproTech / 100-46 / -	PROK2 (prokineticin-2)	Q9HC23		**800** —	-	-	-	May function as an output molecule from the suprachiasmatic nucleus (SCN) that transmits behavioral circadian rhythm. May also function locally within the SCN to synchronize output. Potently contracts gastrointestinal (GI) smooth muscle
				Recombinant Human Prokineticin-2					
43	Prestwick / Prestw-888 / 58-33-3	promethazine	6014		**3979** — 8	51	14	553	Anti-Allergic Agents, Antipruritics, Histamine H1 Antagonists
				Promethazine hydrochloride					
44	SantaCruz / sc-3504 / 53123-88-9	sirolimus	5284616		**914** — 181	491	0	5	Anti-Bacterial Agents, Antibiotics/ Antineoplastic, Antifungal Agents, Immunosuppressive Agents
				Rapamycin					
45	Prestwick / Prestw-167 / -	riluzole hydrochloride	6419992		**4006** — 0	33	4	208	Riluzole is a neuroprotective agent with anticonvulsant, sedative, anxiolytic, anti-ischemic and anesthetic properties. Inhibits glutamate release, enhances glutamate uptake (abcambiotechnologies)
				Riluzole hydrochloride					
46	Prestwick / Prestw-481 / 153-98-0	serotonin hydrochloride	160436		**5901** — 2	16	9	319	Endogenous 5-HT receptor agonist. Neurotransmitter involved in diverse physiological functions such as mood, appetite, sleep, sex and temperature in addition to modulating cardiovascular function and the gastrointestinal system (abcambiotechnologies)
				Serotonin hydrochloride					
47	PeproTech / 100-45 / -	SHH (sonic hedgehog protein)	Q15465		**200** —	-	-	-	Binds to the patched (PTC) receptor, which functions in association with smoothened (SMO), to activate the transcription of target genes. In the absence of SHH, PTC represses the constitutive signaling activity of SMO. Also regulates another target, the gli oncogene. Intercellular signal essential for a variety of patterning events during development: signal produced by the notochord that induces ventral cell fate in the neural tube and somites, and the polarizing signal for patterning of the anterior-posterior axis of the developing limb bud. Displays both floor plate- and motor neuron-inducing activity. The threshold concentration of N-product required for motor neuron induction is 5-fold lower than that required for floor plate induction
				Recombinant Human Sonic Hedgehog (Shh)					
48	SantaCruz / sc-220189 / 81-24-3	taurocholic acid	6675		**51572** — 1	6	0	0	Cholagogues and Choleretics, Detergents
				Taurocholic acid					

Supplementary Table 4. Final selection of 52 stimuli used in the main experiment (to be continued).

LEGEND	Supplier / Catalog # / CAS #	compound name from UniProt, PubChem or other source	compound ID from UniProt or PubChem	compound IMAGE from PubChem, PDB or other source	target concentration we used in ng/ml				Compound Function, Pharmacological Action or general Biological Effect. Sources: UniProt, PubChem, MeSH, other
					active IC50s	total IC50s	active screens	total screens	
					Supplier's name for compound				
49	PeproTech / 100-16A / -	TGFA (protransforming growth factor alpha)	P01135		200				TGF alpha is a mitogenic polypeptide that is able to bind to the EGF receptor/EGFR and to act synergistically with TGF beta to promote anchorage-independent cell proliferation in soft agar.
					-	-	-	-	
					Recombinant Human TGF-α				
50	PeproTech / 300-01A // 400-14 / -	TNFA (tumor necrosis factor)	P01375// P16599		100				Cytokine that binds to TNFRSF1A/TNFR1 and TNFRSF1B/TNFBR. It is mainly secreted by macrophages and can induce cell death of certain tumor cell lines. It is potent pyrogen causing fever by direct action or by stimulation of interleukin-1 secretion and is implicated in the induction of cachexia. Under certain conditions it can stimulate cell proliferation and induce cell differentiation.
					-	-	-	-	
					Recombinant Human//Rat TNF-α				
51	Prestwick / Prestw-856 / 64490-92-2	tolmetin	23677829		3519				Anti-Inflammatory Agents/ Non-Steroidal, Cyclooxygenase Inhibitors
					0	0	0	5	
					Tolmetin sodium salt dihydrate				
52	PeproTech / 120-20 / -	WISP3 (WNT1-inducible-signaling pathway protein 3)	O95389		150				Appears to be required for normal postnatal skeletal growth and cartilage homeostasis.
					-	-	-	-	
					Recombinant Human WISP-3				

Supplementary Table 4. Final selection of 52 stimuli used in the main experiment.