Sepsis is a syndrome with hyperactivity of TH17-like innate immunity and hypoactivity of adaptive immunity

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Abstract

Currently, there are two major theories for the pathogenesis of sepsis: hyperimmune and hypoimmune. Hyperimmune theory suggests that cytokine storm causes the symptoms of sepsis. On the contrary, hypoimmune theory suggests that immunosuppression causes the manifestations of sepsis. By using microarray study, this study implies that hyperactivity of TH17-like innate immunity and failure of adaptive immunity are noted in sepsis patients. Thus, both hyperimmune and hypoimmune play important roles in the pathophysiology of sepsis.

Introduction

Despite of the discovery of antibiotics, mortality rate of sepsis is still very high. Most important of all, the exact pathophysiology of sepsis is still unclear. Currently, there are two dominant theory to explain the etiology of sepsis: hyperimmune theory and hypoimmune theory. However, these two theories are contrary with each other. Hyperimmune theory was proposed by Dr. Lewis Thomas. In his classical paper in NEJM 1972, he proposed that hyperactivation of proinflammatory cytokines, the cytokine storm, is the actual cause of sepsis symptoms. These uncontrolled cytokines destruct and cause multiple organ failure. His theory is the mainstream theory of sepsis etiology. Based on this theory, therapeutic strategy such as antibody neutralizing TNFα was tested in septic patients in clinical trials. However, these antibodies did not improve the survival rate of septic patients. Further, anti-TNFα increased the mortality rate of septic patients in several clinical trials. That makes people to doubt the hyperimmune theory. Thus, another theory-hypoimmune theory emerges. Based on the observation that immunosuppressive patients are prone to get sepsis, hypoimmune status was suggested to be the etiology of sepsis. However, the hypoimmune theory cannot successfully explain the proinflmmatory cytokines storm noted in sepsis. Both hyperimmune theory and hypoimmune theory have clinical and experimental evidences. However, they are contrary with each other. Here, I use the microarray study of whole blood of septic patients to propose a new theory: Sepsis is a syndrome of hyperactivity of innate immunity and hypoactivity of adaptive immunity. This new theory solves the above controversy.

Material and Methods

Microarray dataset

According to Dr. J. A. Howrylak's research in Physiol Genomics 2009, he collected total RNA from whole blood in sepsis and sepsis induced ARDS patients.[1] He tried to find out molecular signature of ARDS compared to sepsis patients. His dataset is available in Gene Expression Omnibus (GEO) www.ncbi.nlm.nih.gov/geo (assession

number GSE 10474). I use his samples of sepsis patients from this dataset to do the further microarray analysis. The sample size is 21 patients with 35% mortality rate. The second dataset is from GSE20189 of Gene Expression Omnibus. This dataset was collected by Dr. Melissa Rotunno in Cancer Prevention Research 2011.[2] Molecular signature of early stage of lung adenocarcinoma was studied by microarray. I use the healthy control (sample size 21)whole blood RNA from this dataset to compare the septic patients. In this study, I perform further analysis to study peripheral leukocyte gene expression profiles of sepsis compared to those of healthy controls.

Statistical analysis

Affymetrix HG-U133A 2.0 genechip was used in both samples. RMA express software(UC Berkeley, Board Institute) is used to do normalization and to rule out the outliners of the above dataset. I rule out the potential outliners of samples due to the following criteria:

1. Remove samples which have strong deviation in NUSE plot

2. Remove samples which have broad spectrum in RLE value plot

3. Remove samples which have strong deviation in RLE-NUSE mutiplot

4. Remove samples which exceed 99% line in RLE-NUSE T2 plot

Then, Genespring XI software was done to analysis the significant expressed genes between ARDS and healthy control leukocytes. P value cut-off point is less than 0.05. Fold changecut-off point is >2.0 fold change. Benjamini-hochberg corrected false discovery rate was used during the analysis. Totally, a genelist of 3277 genes was generated from the HGU133A2.0 chip with 18400 transcripts including 14500 well-characterized human genes.

RT-PCR confirmation

Dr. J. A. Howrylak performed real time PCR for selected transcripts (cip1, kip2) by using TaqMan Gene Expression Assays (Applied Biosystems, Foster City, CA). In the second dataset, Dr. Melissa Rotunno also performed qRT-PCR test to validate the microarray results. RNA quantity and quality was determined by using RNA 600 LabChip-Aligent 2100 Bioanalyzer. RNA purification was done by the reagents from Qiagen Inc. All real-time PCRs were conducted by using an ABI Prism 7000 Sequence Detection System with the designed primers and probes for target genes and an internal control gene-GAPDH. This confirms that their microarray results are convincing compared to RT-PCR results.

Results

RMA analysis of whole blood from healthy normal control

The RMA analysis was performed for RNA samples from whole blood of healthy control of the lung adenocarcinoma dataset. Raw boxplot, NUSE plot, RLE value plot, RLE-NUSE multiplot, and RLE-NUSE T2 plot were generated. Then, sample was included and excluded by using these graphs(Figure 1A, 1B, 1C, 1D, 1E). Because of the strong deviation in the T2 plot, the sample GSM506435 was removed for the further analysis.

RMA analysis of whole blood from septic patients

The RMA analysis was performed for RNA samples from whole blood of sepsis patients dataset. Raw boxplot, NUSE plot, RLE value plot, RLE-NUSE multiplot, and RLE-NUSE T2 plot were generated. Then, sample was included and excluded by using these graphs(Figure 2A, 2B, 2C, 2D, 2E)

Toll-like signaling and heat shock protein expression in septic patients

According to the microarray analysis, Toll-like receptors 1, 2, 4, 5, 8 are up-regulated in sepsis.(Table 1) CD14 molecule and downstream signaling such as IRAK4 and TAB2 are also up-regulated. TLR1, 2, 4, 5, 8 are mediating anti-bacterial immune response. Thus, TH17-like proinflamatory cytokines such as IL-6 will be triggered. However, the negative TLR regulator-IRAK3 is 21 fold up-regulated. Thus, TLR 1, 2, 4, 5, 8 signaling may not successfully trigger proinflammatory cytokines. Other pathway such as CD14 may act as an important alternative pathway to trigger IL-6 and other TH17-like cytokines. Other pattern recognition receptors such as formyl peptide receptors (FPR)which can recognize specific bacterial antigen to trigger innate immunity are also differentially expressed. FPR1 is 7.6 fold down-regulated, but FPR2 is 4.7 fold up-regulated.

In table 2, we can see that many heat shock protein genes are up-regulated. Fever is a usual manifestation of sepsis. Thus, it is not surprising that heat shock proteins are expressed during sepsis. Among them, heat shock protein 70 (HSPA1A/1B) is 7 fold up-regulated. HSP70 can bind to TLR4 to trigger anti-bacterial TH17-like innate immunity. It is worth noting that HSP90AA1 is 13 fold down-regulated. HSP90 can bind to steroid receptor and prevent its action. If HSP90 is down-regulated, the action of steroid cannot be stopped. Thus, steroid related immune regulatory effect

may be initiated during sepsis.

Antigen processing and antigen presentation genes in sepsis

In table 3 and table 4, we can see many cathepsin and proteasome genes are up-regulated. Up-regulated cathepsin genes include CTSA, CTSD, CTSC, CTSG, and CTSZ. But, CTSO and CTSW are down-regulated. Cathepsin W (CTSW) is related to CD8 T cell activation. Up-regulated proteasome genes include PSMD13, PSMC6, PSMD12, PSMD5, PSMB6, and PSMD10. Down-regulated proteasome genes include PSMF1, PSMC2, and PSME4, Among them, PSMF1 is a proteasome inhibitor. Both cathepsins and proteasomes are important in the antigen processing pathways. We can see antigen processing after bacterial infection is intact.

In table 5, however, we can see all MHC related genes are down-regulated in leukocytes of septic patients. These down-regulated genes include HLA-DPB, HLA-DQA, HLA-DRB, HLA-DOB, HLA-DRA, HLA-DQB, Tapasin, MHC I related transcripts, HLA-B, and HLA-DPA. Among them, HLA-B is more than 11 fold down-regulated. MHC genes are keys to the antigen presentation to trigger adaptive immune reaction such as B cell or T cell activation. Since all the MHC related genes are down-regulated, antigen presentation during sepsis is likely to be impaired.

TH17-like innate immune transcription factors in sepsis

In table 6, many immune related transcription factors are differentially regulated during sepsis. First of all, many innate immunity related transcription factors are up-regulated in septic patients. These include AP1(JunB and FosL2), NFIL3, ARNT, and CEBP(CEBPA, CEBPG, and CEBPD) genes. Aryl hydrocarbon receptor nuclear translocator(ARNT) plays an important role in the activation of TH17-like innate immunity. CEBP family genes are related to the activity of myeloid cells and granulocytes. CEBP genes are also related to the activation of acute response proteins. In addition, the inhibitor of NFkB, NFKBIA, is down-regulated in sepsis. It means that the activity of NFkB, an key innate immunity mediator, is up-regulated in septic patients. It is worth noting that two important transcription factors: High Mobility Group Box(HMGB) and Hypoxia inducible factor alpha(HIFα) are also up-regulated during sepsis. HMGB, a vital innate immunity mediator, is greater than nine fold up-regulation.

STAT1, a key transcription factor for TH1 and THαβ immunity, is down-regulated in sepsis. In addition, TBX21(T-bet), a key TH1 immune response driver, is also

down-regulated. (Table 25) In addition, MafB which can suppress IFNαβ in THαβ immunity is up-regulated. Other TH2 related key transcription factors such as GATA3 and C-MAF are also down-regulated. It means that TH1, TH2, and THαβ are down-regulated in sepsis. Surprisingly, key TH17 related transcription factors are also down-regulated including REL, STAT3, and RORA. Besides, SOCS3, a negative regulator of the central TH17 transcription factor STAT3, is up-regulated. It means that TH17 helper cells cannot be successfully triggered. On the other hand, Treg and TGFβ signaling are up-regulated including STAT5B, SMAD2, and SMAD4. Thus, Treg cells are likely to be activated in sepsis. This matches the previous observations that Treg cells are up-regulated during sepsis.

TH17-like and Treg related cytokines are up-regulated during sepsis

In table 7, many TH17-like and Treg related cytokines are up-regulated in septic patients. The whole TGFβ activation machinery is up-regulated including thrombospondin, CD36, and TGFβ itself. TGFA is also up-regulated. Besides, IL-6 is also up-regulated in sepsis. Thus, both key TH17 driven cytokines, TGFβ and IL-6, are activated in septic patients. However, full activation of TH17 helper cells also need a TCR signaling. IL-32, a TH1 related macrophage differentiation factor, is

down-regulated. TH22 mediators, IL1A is down-regulated and IL1RN (IL1 receptor antagonist is up-regulated. It means that TH22 is not activated in sepsis.

In table 8, cytokine receptors are differentially regulated in sepsis. On the contrary with cytokine, cytokine in a certain immunological pathway is usually down-regulated. Thus, since TH17-like immunity is activated. TGFBR3, IL6R, and IL17RA are all down-regulated. TGFβ receptor 3 is greater than 11 fold down-regulated, and interleukin 6 receptor is greater than 16 fold down-regulated. Treg is also triggered in sepsis, so TGFBR3, IL2RB, and IL7R are also down-regulated. TH1 related cytokine receptors, IFNGR1 and IFNGR2, are up-regulated. TH2 cytokine receptor, IL4R, is also up-regulated. As for THαβ immunity, IFNAR1 is up-regulated but IFNAR2 is down-regulated. TH22 cytokine receptors, IL1R1 and IL1R2, are up-regulated. Thus, TH1, TH2, THαβ, and TH22 are not activated during sepsis.

In table 9, important CSF receptors are up-regulated. These include CSF2 (GM-CSF) receptor α and β. GM-CSF can promote the proliferation of monocyte and granulocyte lineages. In table 10, many TNF related genes are differentially regulated. Up-regulated TNF related genes include TNFAIP6, TNFAIP8, TNFRSF1A and TNFSF10. Down-regulated TNF related genes include TNFRSF10C, TNFRSF9, and TNFSF14.

TNFRSF1A is the major receptor of TNFα. Thus, both IL-1 receptor and TNFα receptor are up-regulated during sepsis. TNFSF10(TRAIL) is a pro-apoptotic factor, and TNFRSF10C is a receptor to prevent TRAIL induced apoptosis. Thus, TRAIL induced apoptosis pathway is activated in sepsis. TNFRSF9(4-1BB) and TNFSF14(CD258) are both important lymphocyte co-stimulatory molecules. Thus, lymphocyte costimulation is likely to be impaired at sepsis.

TH17 related chemokine up-regulation during sepsis

In table 11, we find out that TH17 related chemokine are up-regulated in septic patients. These chemokines include S100 binding proteins (S100A11, S100A8, S100A9, and S100P), CCR2(neutrophil chemokine receptor), hyaluronan-mediated motility receptor (HMMR), and chemokine-like factor(CKLF). THαβ related chemokine factors such as CX3CR1, XCL1, and XCL2 for NK cell recruitment are down-regulated. TH1 related chemokine factors such as CCL4 and CCR1 for macrophage/monocyte recruitment are also down-regulated. Besides, TH2 chemokine receptor CCR3 for eosinophil recruitment is also down-regulated. It is worth noting that CCR7, the chemokine receptor for central memory T cells, is greater than 5 fold down-regulated in sepsis. Thus, the generation of central memory T cell is likely to be impaired during

sepsis.

In table 12, many prostaglandin and leukotriene genes are differentially regulated. Prostaglandins and leukotrienes are important chemotaxis mediators. The key enzyme: leukotriene A4 hydrolase for synthesizing leukotriene B4, a potent PMN chemoattractant, is up-regulated. Besides, leukotriene B4 receptor is also up-regulated. Besides, the receptor of PGD2, a TH2 related effector molecule, is 10 fold down-regulated. Prostangin D synthetase is also down-regulated. In addition, the gene 15-hydroxyprostaglandin dehydrogenase (HPGD), which is responsible for shutting down prostaglandin, is 16 fold up-regulated. Key molecules including phospholipase A 2 and arachidonate 5-lipoxygenase to initiate leukotriene synthesis are also up-regulated in sepsis.

Th17-like innate immunity related effector molecule up-regulation in sepsis

In table 13, many acute response proteins are up-regulated. These acute phase proteins are up-regulated by IL-6 and CEBP proteins. These genes include amyloid proteins (APP and APLP2), pentraxin(PTX3), transferrin receptor(TFRC), CLEC (CLEC5A and CLEC1B), and defensins (DEFA1, DEFA1B, DEFA3, and DEFA4). These above proteins are innate immunity effector proteins to attack bacterial antigens

non-specifically. Defensin A4 is greater than 6 fold up-regulated.

In table 14, the whole set complement machinery, an important effector component of innate immunity, is up-regulated. These include CD59, CD55, C1QB, ITGAM, CR1, CD46, C3AR1, ITGAX, C1QA, C1RL, C5AR1, and CD97. Thus, complement molecules are activated during sepsis. These complement molecules attack bactrerial cell walls and membranes to cause their damage. However, complements may also cause harmful effect to the host.

In table 15, certain genes related to PMN phagocytosis and bacteria killing are up-regulated. Neutrophil cytosolic factor 1&4, the subunit of NADPH oxidase for ingested bacteria killing, are up-regulated in sepsis. Carboxypeptidase D (CPD), which can up-regulate nitric oxide, is also up-regulated during sepsis. Nitric oxide is also a key effector molecule for ingested bacteria killing. CPD is greater than 6.9 fold up-regulated.

In table 16, PMN matrix metallopeptidases(MMP) and elastase are up-regulated. These protein enzymes can digest bacterial antigens as well as extracellular matrix. These genes include MMP8, MMP9, MMP25, and ELANE(elastase). In addition, tissue inhibitor of MMP, TIMP2, and serum inhibitors of elastase or proteinase, SERPINA1, SERPINB1, and SERPINB2, are also up-regulated. It means that PMN proteinases are dysregulated. It is worth noting that MMP8 is 32 fold up-regulated and MMP9 is 10

fold up-regulated.

In table 17, apoptosis machinery is up-regulated during sepsis. Up-regulated genes include casapase3, FAS, caspase5, program cell death 10(PDCD10), caspase 1, caspase4, and TRAIL. Down-regulated genes include CFLAR and FAIM3, both of which are apoptosis negative regulators. Thus, apoptosis is activated at sepsis. It matches previous observations that there is massive leukocyte-lymphocyte apoptosis during sepsis.

In table 18, many Fc receptor genes which mediate macrophage and neutrophil phagocytosis are up-regulated. These genes include IgG Fc receptor IIa(FCGR2A), IgE Fc receptor Ig(FCER1G), IgA Fc receptor(FCAR), IgG Fc receptor IIc(FCGR2C), IgG Fc receptor Ib, and IgG Fc receptor Ia/Ic(FCGR1A/1C). Besides, TH2 immunity related IgE Fc receptor Ia is 3.8 fold down-regulated. In addition, THαβ immunity related CD16 IgG Fc receptor expression is unchanged. TH17-related innate immunity is mediated by IgG(IgG2/IgG3) and IgA. Thus, TH17-like innate immunity with enhanced phagocytosis is noted during sepsis.

In table 19, many CD molecules are up-regulated or down-regulated during sepsis. These CD molecules are important immune response mediators. Among them, up-regulation of CD36, the thrombospodin receptor, means that TGFβ molecule is also up-regulated. Down-regulated CD2 molecule means that T cell activation

pathway is impaired. In addition, down-regulation of CD40 means that activation of antigen presenting cells such as B cells is impaired. Besides, CD24 is usually down-regulated in memory B cells. However, during sepsis, CD24 is strongly up-regulated.

Coagulation , glycolysis, acidosis, and vasodilation gene dysregulation in sepsis

In table20, many coagulation related genes are dysregulated during sepsis. Actually, disseminated intracellular coagulopathy is a common manifestation of sepsis. Up-regulated coagulation genes include factor XIII(F13A1), factor V(F5), factor VIII(F8),platelet glycoprotein Ib(GP1BB), Protein S(PROS1), Plasminogen activator(PLAUR), multiple coagulation deficiency 2(MCFD2), tissue factor pathway inhibitor(TFPI), factor II receptor-like(F2RL1), integrin alpha 2b(ITGA2B), PDGF-C, integrin beta 3(ITGB3), and thrombomodulin(THBD). Down-regulated coagulation related genes are Plasmigogen-like A, B1, and B2(PLGLA, PLGLB1 and PLGLB2). PDGF-C is nine fold up-regulated, and GP1BB is 5 fold up-regulated.
Sepsis is also related to lactate acidosis, and glycolysis activity is usually risen during sepsis. In table 21, we can see the whole enzyme set of glycolytic pathway is up-regulated. These genes include lactate dyhydrogenase A(LDHA), phosphoglycerate

kinase 1 (PGK1), pyruvate kinase (PKM), 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase3 (PFKFB3), hexokinase 2 (HK2), glycogen phosphorylase (PYGL), 2,3-bisphosphoglycerate mutase (BPGM), hexokinase 3 (HK3), glucose-6-phosphate isomerase (GPI), 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase2 (PFKFB2), glyceraldehyde-3-phosphate dehydrogenase (GAPDH), and enolase1 (ENO1). PFKB3 is seven fold up-regulated, and PFKB2 is 11 fold up-regulated. Pyruvate dehydrogenase kinase which can stop pyruvate from forming acetyl-CoA to enter aerobic citric acid cycle is up-regulated. Pyruvate dehyrogenase phosphatase which can help pyruvate to form acetyl-CoA to enter aerobic citric acid cycle is down-regulated. Thus, lactate genesis is up-regulated at sepsis.

Besides, many H^+-ATPase genes are also up-regulated. In my previous article, I found a coupling between glycolytic enzymes and H^+-ATPases to facilitate acidosis. In table 22, up-regulated H^+-ATPase genes include ATP6V08, ATP6V0E1, ATP6AP2, ATP6V1C1, TCIRG1, ATP6V1D, ATP11B, and ATP11A. In addition, the enzymes to generate H_2CO_3, carbonic anhydrase II and IV, are also up-regulated. Carbonic anhydrase IV is greater than seven fold up-regulated. Combining the effect of lactate production and up-regulation of H^+-ATPase activity, septic acidosis can be explained.

Septic shock is a common sequel of sepsis. Here, I find out several genes which can

mediate vasodilation are up-regulated during sepsis. These genes include angiotensinase C (PRCP), adrenomedullin (ADM), and monoamine oxidase A (MAOA) in table23. PRCP can digest angiotensin, a key hypertensive agent, to cause vasodilation. Adrenomedullin is also a vasodilator. MAO-A, which is the enzyme to metabolize norepinephrine and epinephrine, is also up-regulated during sepsis. This can help to explain why septic shock occurs.

Failure of T cell adaptive immunity during sepsis

In table 24, we can see many THαβ related NK cell genes are down-regulated. These genes include killer cell receptors(NKTR, KLRK1, LAIR2, KLRD1, KLRG1, KLRB1, and KLRF1), granzymes(GZMA,GZMK,GZMM, GZMB, and GZMH) and perforin(PRF1). NKTR is greater than 26 fold down-regulated. Thus, THαβ immunity is not activated during sepsis.

Strikingly, I find out that all the T cell related genes are down-regulated during sepsis in table 25. These down-regulated genes include T cell specific transcription factors (IKZF1(ikaros), TCF7, NFAT5, TCF7L2, NFATC2IP, TBX21(T-bet), and ID2), co-stimulatory molecules(CD3E, CD8A, CD3G, LY9, CD3D, and CD2), TCR related genes(TRAC, TARP, TRBC1, TRBC1/C2, TRD@, TRGC2, and TRDV3), granzymes/perforins(GZMA, GNLY, GZMK, GGZMM, GZMB, GZMH, PRF1), and T cell activation signaling(ZAP70 and LCK).

Thus, T cell adaptive immunity is impaired in sepsis. Septic patients cannot successfully induce T cell response against the extracellular bacteria. That explains why immune-compromised individuals are easily suffering from sepsis.

In table 26, many B cell related genes are differentially regulated. Up-regulated genes include transcription factor BCL6, immunoglobin light chains(IGK, IGJ, IGLV1-44, and IGKV1-5), and immunoglobin heavy chain(IGH-G1, IGH-G2, IGH-A1, and IGH-A2). Down-regulated genes include B cell transcription factors (PAX5 and IKZF1), immunoglobin heavy chain(IGH-M) and B cell activation signaling (CD40, FYN and LYN). Since TGFβ can cause B cell isotype switch to IgG2 and IgA, this may explain our findings. The key antibacterial immunoglobin-IgM is down-regulated. The key BCR as well as TCR activation signaling is via PI3 kinase. However, the PI3 kinase related genes are down-regulated(PI3KR1, PI3KCB, PI3KCG, and PI3KIP1), and the negative regulator of PI3K-PTEN is greater than 5 fold up-regulated. So, the main B cell specific transcription factors and activation signaling are not activated. That means that B cells are not fully activated.

Figure legends

Figure 1. RMA express plot for selecting samples in normal healthy controls.

1-A NUSE boxplot for normal control

1-B RLE boxplot for normal control

1-C RLE-NUSE multiplot for normal control

1-D RLE-NUSE T2 plot for normal control

1-E Raw data Boxpolt for normal control

Figure 2. RMA express plot for selecting samples in septic patients.

2-A NUSE boxplot for septic patients

2-B RLE boxplot for septic patients

2-C RLE-NUSE multiplot for septic patients

2-D RLE-NUSE T2 plot for septic patients

2-E Raw data Boxplot for septic patients

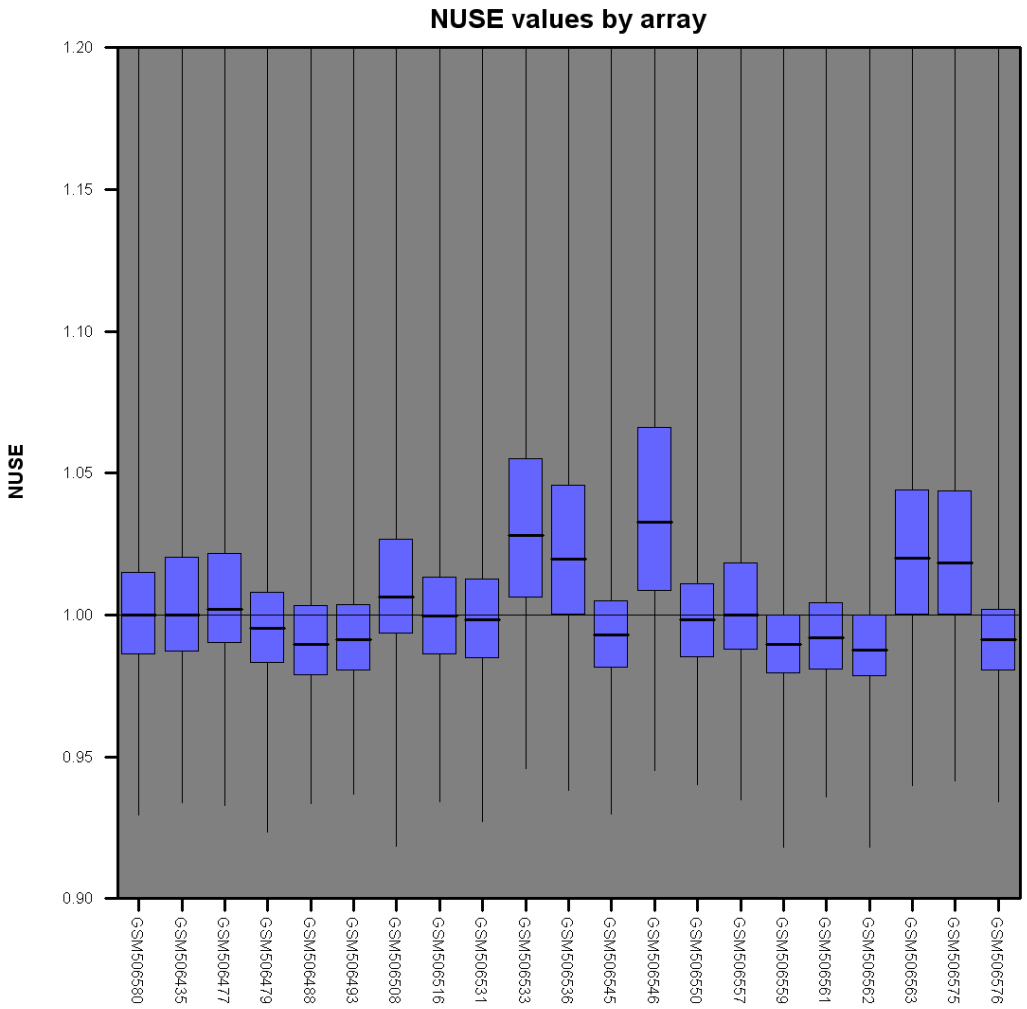
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Figure 1A

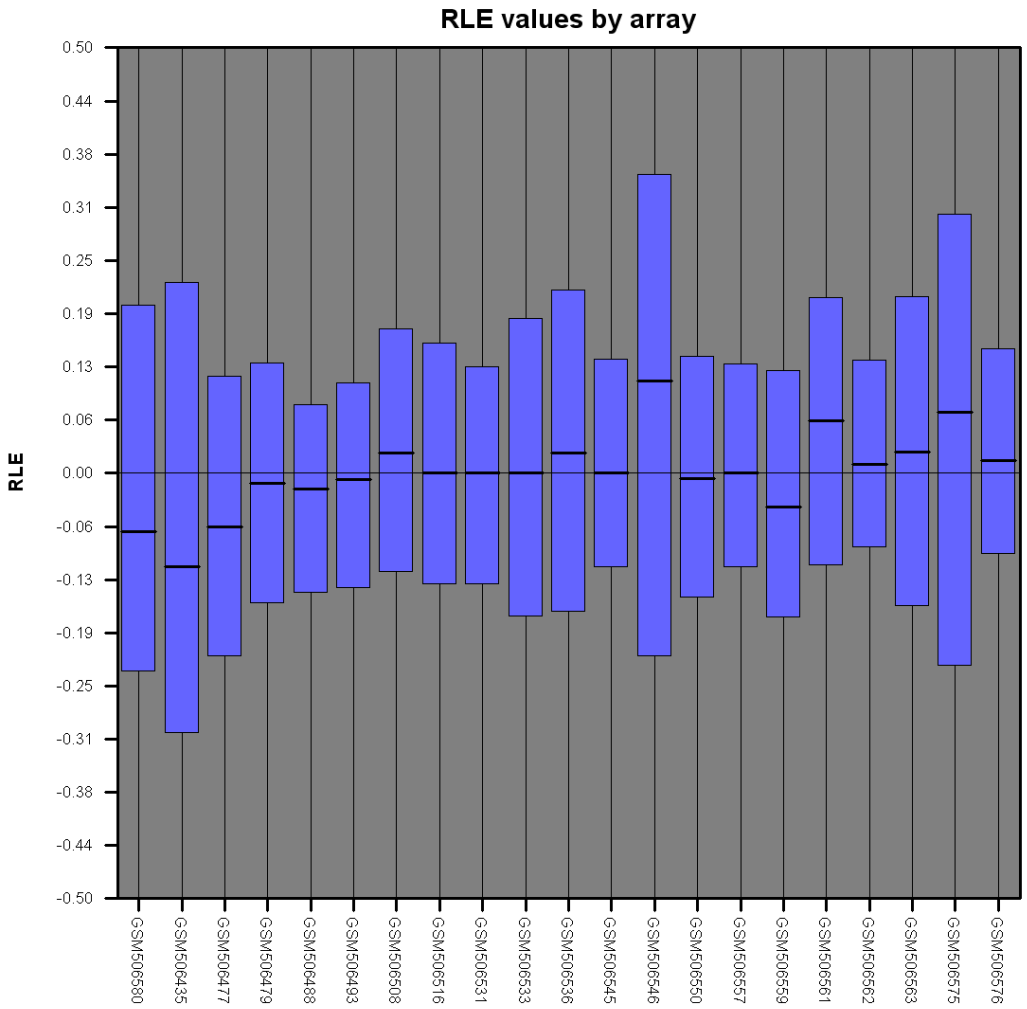
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Figure 1-B

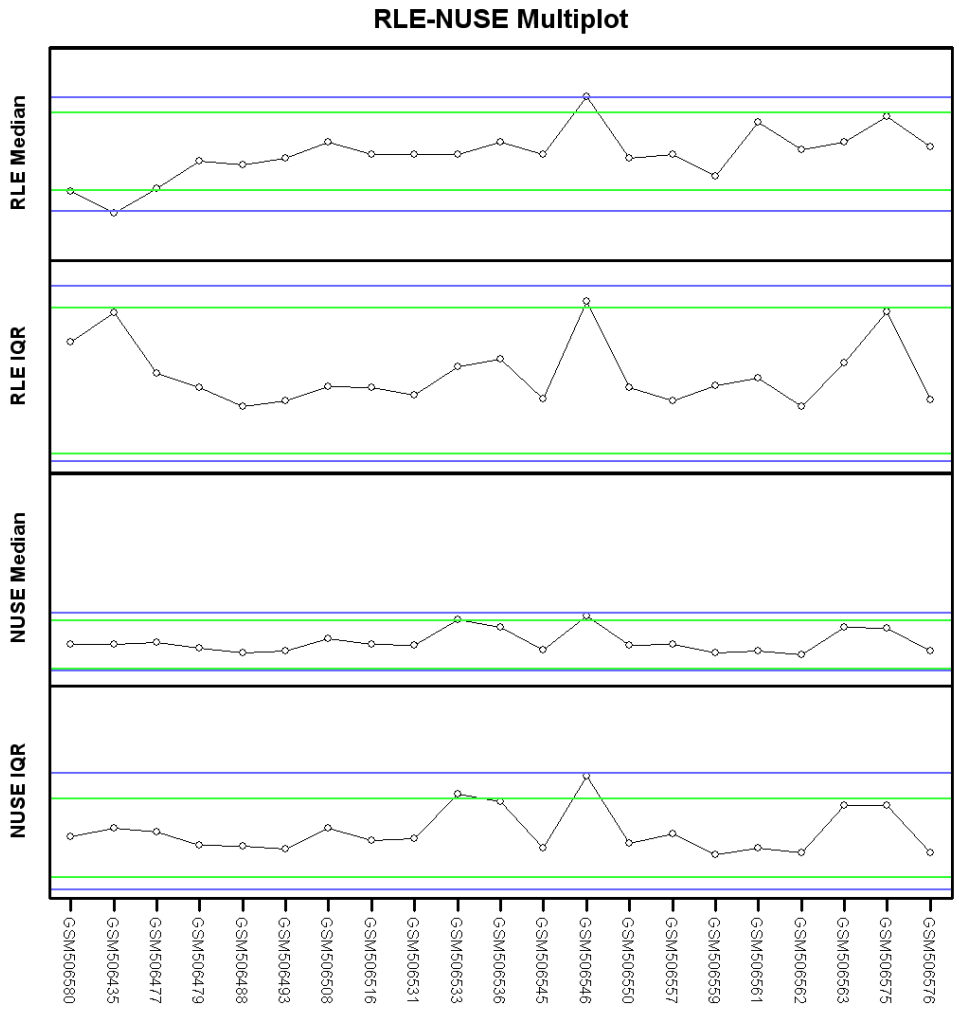
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Figure 1-C

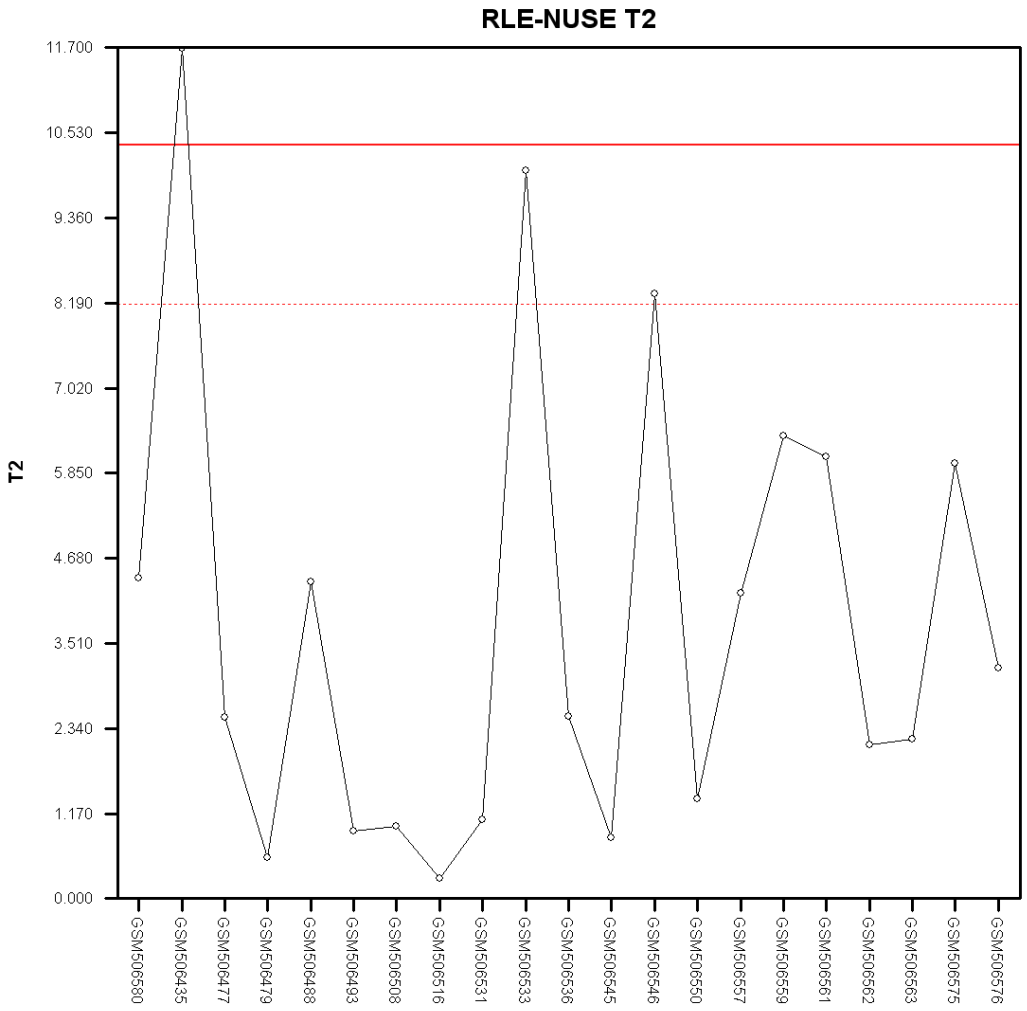
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Figure 1-D

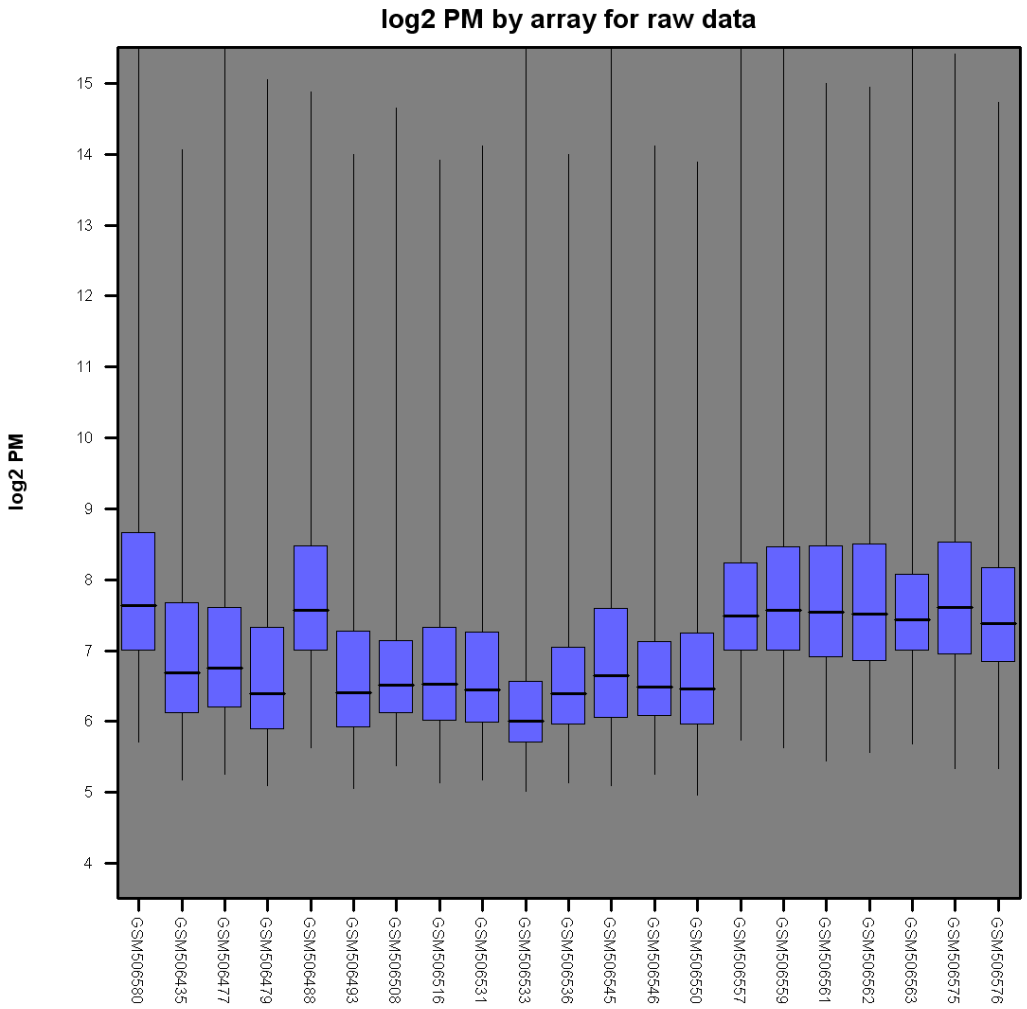
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Figure 1-E

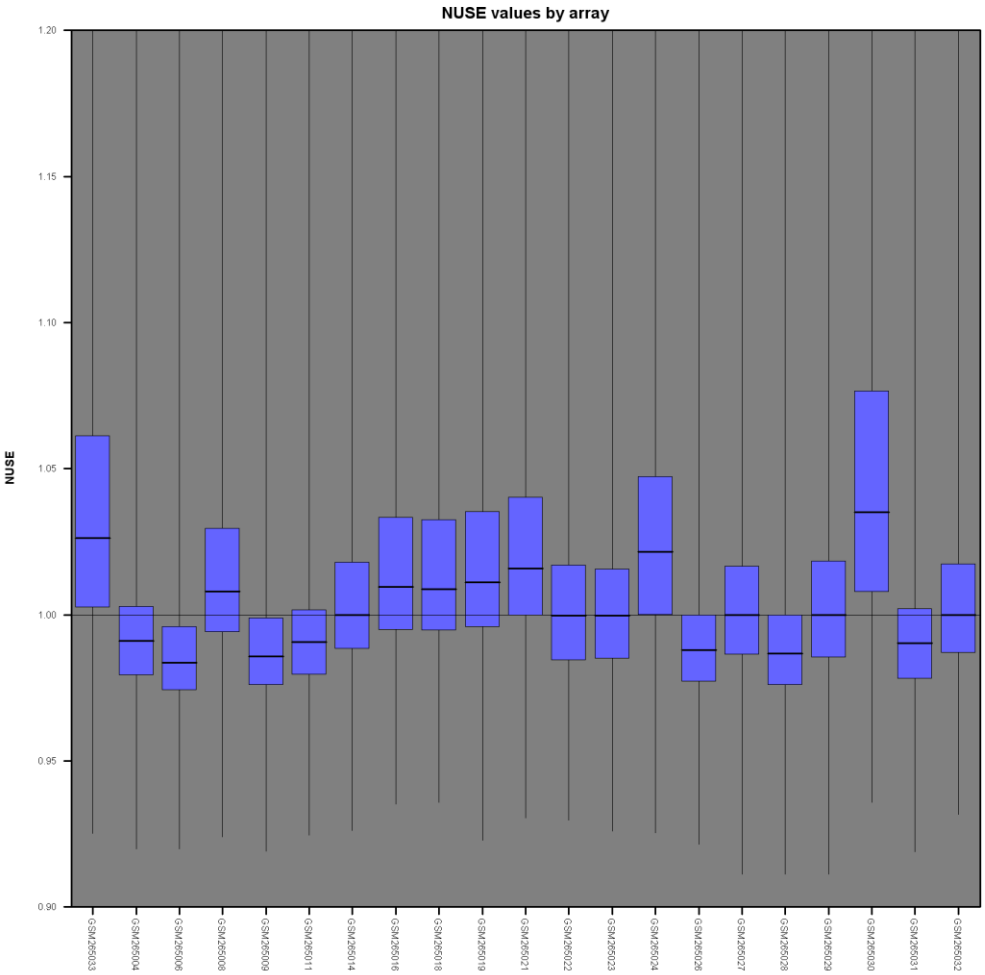
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Figure 2-A

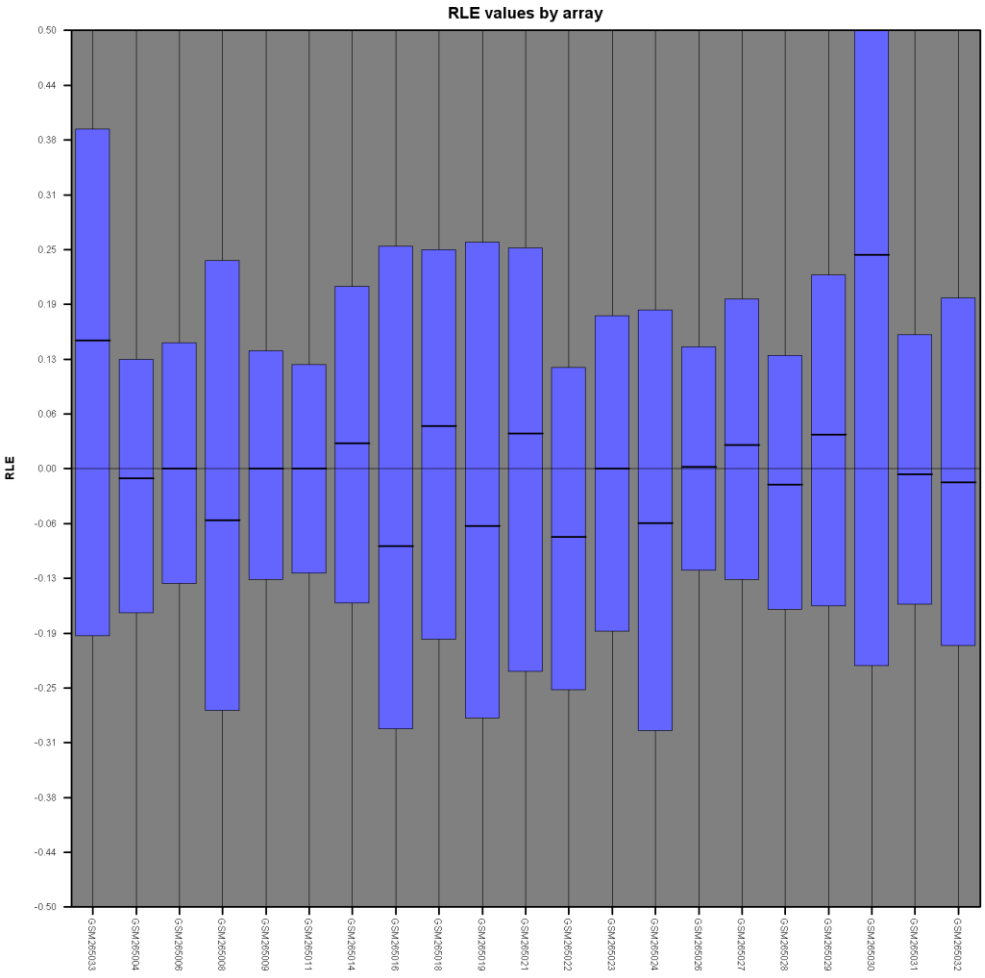
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Figure 2-B

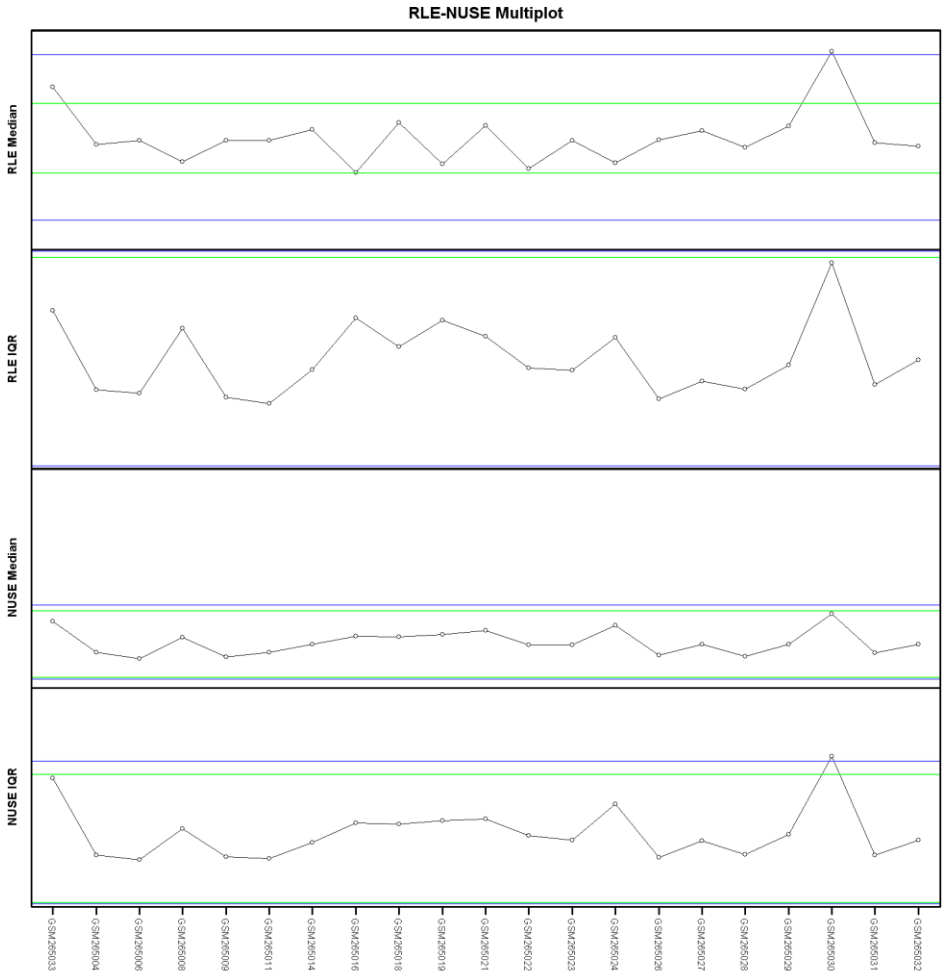
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Figure 2-C

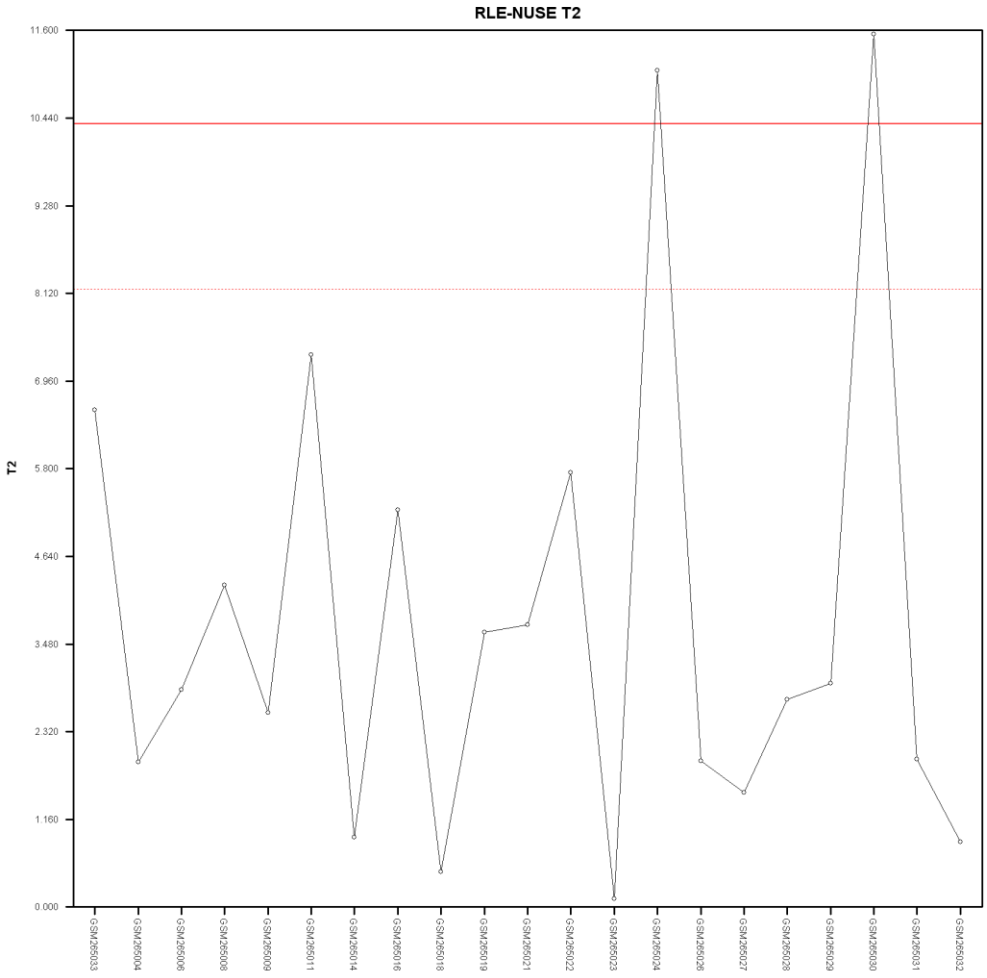
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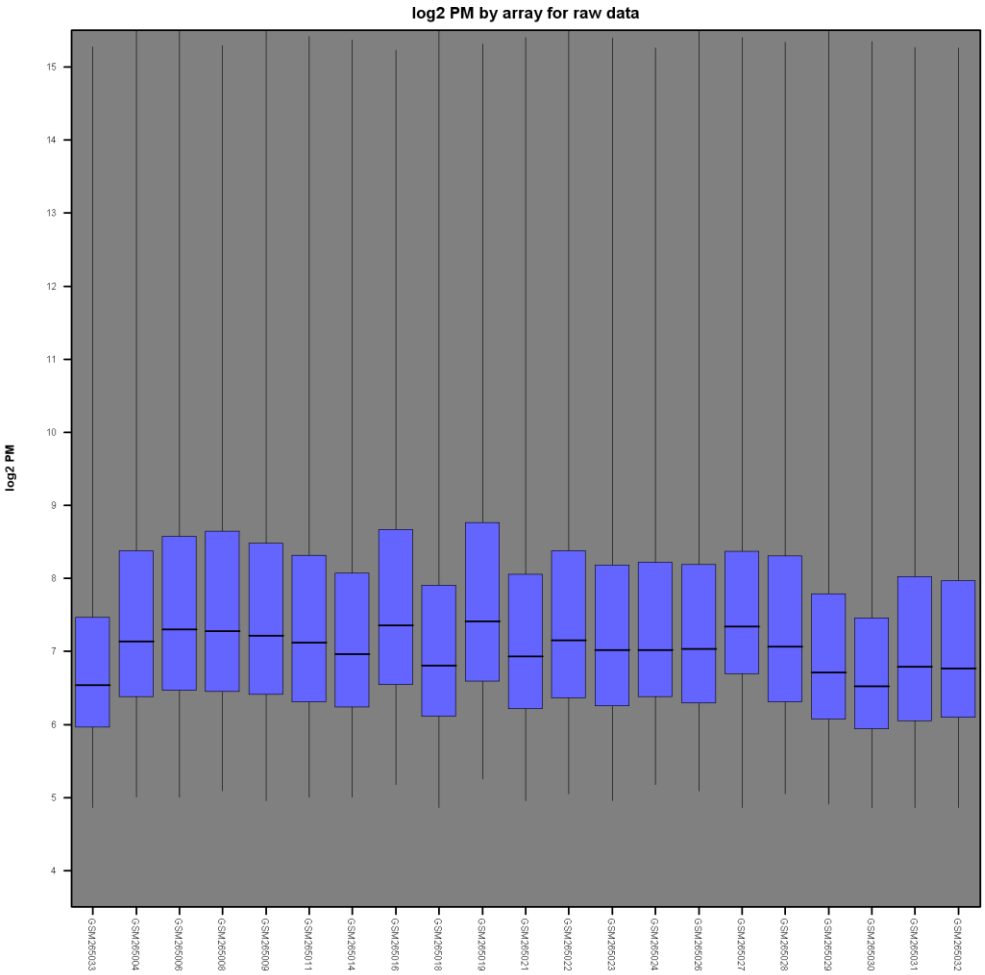
Figure 2-D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GSM265032

Figure 2-E

Table 1. TLR

Probe ID	Pvalue	Arrow	Fold	Gene
201743_at	1.37E-04	up	2.176301	CD14
204924_at	1.45E-10	up	3.380896	TLR2
210166_at	9.16E-08	up	2.395743	TLR5
210176_at	0.001131	up	2.073326	TLR1
213817_at	3.14E-13	up	21.0364	IRAK3
219618_at	1.89E-09	up	2.692996	IRAK4
220832_at	4.76E-09	up	5.164016	TLR8
221060_s_at	6.62E-07	up	3.331681	TLR4
212184_s_at	2.03E-05	up	2.61743	TAB2
221705_s_at	8.46E-10	down	2.07506	SIKE1
205118_at	1.05E-10	down	7.612908	FPR1
210772_at	2.06E-08	up	4.776773	FPR2
210773_s_at	2.95E-06	up	4.516464	FPR2

Table 2. HSP

Probe ID	Pvalue	Arrow	Fold	Gene
200598_s_at	4.02E-04	down	2.112279	HSP90B1
200599_s_at	6.27E-04	up	2.143909	HSP90B1
200800_s_at	8.98E-09	up	2.664816	HSPA1A /1B
200941_at	1.29E-10	up	2.175182	HSBP1
200942_s_at	7.06E-08	up	2.197023	HSBP1
202557_at	1.10E-05	up	2.82175	HSPA13
202558_s_at	7.12E-05	up	2.112017	HSPA13
202581_at	1.98E-14	up	7.20045	HSPA1A/1B
202842_s_at	6.81E-06	up	2.73954	DNAJB9
202843_at	8.03E-07	up	2.087716	DNAJB9
206782_s_at	1.21E-09	up	2.374709	DNAJC4
208810_at	3.57E-04	up	2.196654	DNAJB6
209015_s_at	9.66E-09	up	2.548422	DNAJB6
209157_at	1.97E-10	up	2.893105	DNAJA2
210338_s_at	1.85E-05	down	2.06926	HSPA8
211936_at	1.05E-07	up	2.110743	HSPA5
211969_at	3.39E-17	down	13.51482	HSP90AA1
212467_at	1.01E-07	up	3.702917	DNAJC13
212911_at	1.88E-13	up	3.009307	DNAJC16
219237_s_at	2.18E-04	down	2.275608	DNAJB14

Table 3. Cathepsin

Probe ID	Pvalue	Arrow	Fold	Gene
200661_at	6.28E-10	up	2.550876	CTSA
200766_at	3.53E-12	up	3.746886	CTSD
201487_at	7.15E-06	up	2.584763	CTSC
203758_at	4.23E-08	down	2.3372	CTSO
205653_at	1.36E-04	up	3.234722	CTSG
210042_s_at	2.94E-07	up	3.044302	CTSZ
214450_at	2.16E-06	down	2.202781	CTSW

Table 4. Proteasome

Probe ID	Pvalue	Arrow	Fold	Gene
201052_s_at	8.16E-06	down	2.218188	PSMF1
201067_at	3.68E-20	down	4.692738	PSMC2
201232_s_at	5.58E-11	up	2.577756	PSMD13
201699_at	2.88E-08	up	4.61153	PSMC6
202352_s_at	1.45E-08	up	2.49783	PSMD12
202353_s_at	1.04E-07	up	2.4536	PSMD12
202753_at	6.55E-08	up	2.001992	PSMD6
203447_at	1.23E-10	up	2.450336	PSMD5
208805_at	6.04E-05	up	2.094127	PSMA6
208827_at	4.41E-09	up	2.513269	PSMB6
212220_at	1.31E-09	down	3.309962	PSME4
219485_s_at	1.85E-07	up	2.271658	PSMD10

Table 5. MHC

Probe ID	Pvalue	Arrow	Fold	Gene
201137_s_at	5.80E-04	down	2.085101	HLA-DPB1
203290_at	2.56E-08	down	5.193201	HLA-DQA1
204670_x_at	6.77E-08	down	2.848446	HLA-DRB1/B4
205671_s_at	1.27E-04	down	2.016965	HLA-DOB
208306_x_at	1.53E-06	down	2.437791	HLA-DRB1
208894_at	8.06E-07	down	2.762713	HLA-DRA
209312_x_at	1.24E-06	down	2.674953	HLA-DRB1/B4/B5
209823_x_at	8.65E-04	down	2.083243	HLA-DQB1
210294_at	7.08E-10	down	2.247553	TAPBP
210528_at	1.28E-05	down	2.565486	MR1
210982_s_at	4.46E-05	down	2.140575	HLA-DRA
211944_at	5.60E-22	down	7.377162	BAT2L2
211947_s_at	9.14E-14	down	4.692785	BAT2L2
211948_x_at	3.66E-28	down	11.74736	BAT2L2
211990_at	5.10E-06	down	3.188215	HLA-DPA1
211991_s_at	1.47E-05	down	2.428313	HLA-DPA1
212384_at	8.83E-15	down	2.983359	HLABAT1
212671_s_at	0.002545	down	2.265915	HLA-DQA1/A2
213537_at	7.83E-05	down	2.338689	HLA-DPA1
214052_x_at	4.45E-14	down	2.404988	BAT2L2
214055_x_at	1.16E-24	down	9.415468	BAT2L2
215193_x_at	2.90E-06	down	2.522364	HLA-DRB1/B3/B4
221491_x_at	1.50E-06	down	2.247077	HLA-DRB1/B3/B4/B5

Table 6. Transcription factor

Probe ID	Pvalue	Arrow	Fold	Gene
M97935_MA_at	1.92E-04	down	2.010955	STAT1
201473_at	3.65E-09	up	2.459731	JUNB
201502_s_at	9.16E-07	down	2.364327	NFKBIA
202527_s_at	5.77E-09	up	3.237444	SMAD4
203075_at	3.46E-06	up	2.133481	SMAD2
203077_s_at	4.90E-07	up	2.370214	SMAD2
203574_at	4.37E-10	up	5.176725	NFIL3
204039_at	4.62E-08	up	2.059098	CEBPA
204203_at	9.92E-07	up	2.172468	CEBPG
205026_at	1.66E-09	up	2.20184	STAT5B
205841_at	1.02E-13	up	4.655113	JAK2
205842_s_at	6.01E-07	up	2.878639	JAK2
206035_at	7.43E-10	down	2.106359	REL
206036_s_at	8.46E-12	down	4.746634	REL
206359_at	3.22E-07	up	2.092249	SOCS3
206363_at	9.68E-06	down	2.261549	MAF
208991_at	1.49E-13	down	3.223685	STAT3
209604_s_at	2.74E-19	down	6.546836	GATA3
209969_s_at	2.12E-08	down	4.748202	STAT1
210426_x_at	1.14E-12	down	6.358444	RORA
210479_s_at	5.21E-15	down	7.850211	RORA
212501_at	1.73E-07	up	2.169912	CEBPB
212549_at	7.00E-12	up	2.369991	STAT5B
212550_at	7.19E-10	up	2.522143	STAT5B
213006_at	6.03E-10	up	4.206962	CEBPD
218221_at	1.49E-11	up	2.349603	ARNT
218559_s_at	9.49E-07	up	3.354582	MAFB
218880_at	5.34E-11	up	3.750719	FOSL2
208808_s_at	1.07E-11	up	9.120556	HMGB
200989_at	1.17E-06	up	2.997033	HIF1A

Table 7. Cytokine

Probe ID	Pvalue	Arrow	Fold	Gene
201108_s_at	2.84E-06	up	2.858913	THBS1
201109_s_at	3.87E-05	up	3.674066	THBS1
201110_s_at	2.02E-09	up	8.271206	THBS1
203085_s_at	1.57E-08	up	2.327314	TGFB1
203828_s_at	7.88E-05	down	2.130993	IL32
205016_at	8.33E-10	up	4.855893	TGFA
205992_s_at	4.40E-06	up	3.5756	IL15
208114_s_at	7.75E-20	down	5.849659	ISG20L2
208200_at	3.06E-11	down	4.80094	IL1A
212195_at	3.90E-06	up	2.667476	IL6ST
206488_s_at	1.04E-04	up	2.926877	CD36
209555_s_at	2.87E-05	up	3.18128	CD36
212657_s_at	2.96E-07	up	2.31195	IL1RN

Table 8. Cytokine receptor

Probe ID	Pvalue	Arrow	Fold	Gene
201642_at	1.42E-09	up	2.315	IFNGR2
202727_s_at	1.44E-08	up	3.323753	IFNGR1
202948_at	5.77E-10	up	6.463163	IL1R1
203233_at	2.36E-10	up	3.270304	IL4R
204191_at	2.98E-07	up	2.05704	IFNAR1
204731_at	7.48E-21	down	11.93166	TGFBR3
204786_s_at	5.23E-19	down	6.864011	IFNAR2
205227_at	2.89E-05	up	2.68359	IL1RAP
205291_at	2.89E-08	down	2.442178	IL2RB
205403_at	1.87E-08	up	6.689801	IL1R2
205707_at	1.73E-09	down	2.408515	IL17RA
205798_at	2.48E-24	down	31.78504	IL7R
205926_at	1.06E-09	down	2.187688	IL27RA
205945_at	1.49E-22	down	16.68902	IL6R
206618_at	4.70E-09	up	12.92154	IL18R1
207072_at	5.22E-08	up	4.927116	IL18RAP
211372_s_at	1.76E-08	up	10.6815	IL1R2
211676_s_at	6.66E-09	up	4.607373	IFNGR1
217489_s_at	2.79E-14	down	3.546462	IL6R

Table 9. CSF

Probe ID	Pvalue	Arrow	Fold	Gene
205159_at	1.17E-06	up	2.511396	CSF2RB
210340_s_at	4.36E-10	up	2.295372	CSF2RA

Table 10. TNF

Probe ID	Pvalue	Arrow	Fold	Gene
202509_s_at	1.99E-12	down	2.4938	TNFAIP2
206026_s_at	7.48E-06	up	3.620447	TNFAIP6
206222_at	1.55E-06	down	2.076582	TNFRSF10C
207536_s_at	5.06E-07	down	2.86682	TNFRSF9
207643_s_at	3.72E-12	up	2.681254	TNFRSF1A
207907_at	9.40E-17	down	3.895788	TNFSF14
208296_x_at	2.21E-05	up	2.431529	TNFAIP8
210260_s_at	4.11E-05	up	2.505209	TNFAIP8
214329_x_at	1.19E-04	up	2.324046	TNFSF10

Table 11. Chemokine

Probe ID	Pvalue	Arrow	Fold	Gene
200660_at	9.23E-12	up	2.053883	S100A11
202917_s_at	2.79E-12	up	2.617102	S100A8
203535_at	3.98E-16	up	2.584441	S100A9
204103_at	3.51E-09	down	2.364728	CCL4
204351_at	7.20E-04	up	2.155134	S100P
205099_s_at	6.98E-05	down	2.455516	CCR1
205863_at	7.49E-14	up	4.166398	S100A12
205898_at	6.76E-04	down	2.496165	CX3CR1
206337_at	5.73E-08	down	5.099034	CCR7
206366_x_at	1.36E-09	down	3.847104	XCL1
206978_at	7.29E-05	up	2.362277	CCR2
207165_at	6.52E-05	up	2.285972	HMMR
208304_at	4.88E-05	down	3.621386	CCR3
214370_at	5.04E-06	down	2.084171	S100A8
214567_s_at	8.06E-08	down	2.902829	XCL1 /// XCL2
221058_s_at	1.49E-09	up	2.15809	CKLF

Table 12. PGD LTX

Probe ID	Pvalue	Arrow	Fold	Gene
203913_s_at	1.26E-08	up	16.54476	HPGD
203914_x_at	3.77E-08	up	14.66064	HPGD
204445_s_at	2.84E-06	up	2.076126	ALOX5
204446_s_at	1.01E-07	up	2.0434	ALOX5
204748_at	0.019719	up	2.109052	PTGS2
205128_x_at	5.85E-07	up	2.664767	PTGS1
207206_s_at	1.59E-04	up	2.531166	ALOX12
209533_s_at	3.14E-10	up	2.619734	PLAA
210128_s_at	9.02E-10	up	2.505719	LTB4R
210145_at	1.51E-12	up	3.476688	PLA2G4A
211548_s_at	4.38E-08	up	12.3211	HPGD
211549_s_at	3.53E-04	up	2.6726	HPGD
211748_x_at	1.56E-06	down	2.033312	PTGDS
214366_s_at	5.17E-10	up	3.681805	ALOX5
215813_s_at	1.01E-08	up	3.363031	PTGS1
215894_at	2.35E-14	down	10.40363	PTGDR
216388_s_at	9.35E-07	up	2.104241	LTB4R
208771_s_at	4.07E-08	up	2.455806	LTA4H

Table 13. Acute Response Protein

Probe ID	Pvalue	Arrow	Fold	Gene
200602_at	3.75E-12	up	4.384286	APP
206157_at	8.31E-08	up	3.272863	PTX3
208248_x_at	2.42E-09	up	2.54326	APLP2
208691_at	0.001264	up	2.485756	TFRC
208702_x_at	7.55E-09	up	2.826174	APLP2
208703_s_at	1.26E-07	up	3.047052	APLP2
208704_x_at	1.61E-08	up	2.435629	APLP2
211404_s_at	4.34E-10	up	2.927751	APLP2
214875_x_at	1.32E-08	up	2.761566	APLP2
214953_s_at	8.93E-05	up	2.120433	APP
219890_at	1.43E-12	up	7.827181	CLEC5A
220496_at	2.59E-07	up	3.327139	CLEC1B
205033_s_at	1.17E-05	up	4.788064	DEFA1/A1B/A3
207269_at	2.87E-05	up	6.665461	DEFA4

Table 14. Complement

Probe ID	Pvalue	Arrow	Fold	Gene
200983_x_at	7.97E-09	up	3.370908	CD59
200984_s_at	9.06E-10	up	3.891589	CD59
200985_s_at	4.85E-11	up	6.593943	CD59
201925_s_at	2.14E-07	up	5.613841	CD55
201926_s_at	6.74E-09	up	3.830297	CD55
202953_at	7.01E-06	up	2.526228	C1QB
205786_s_at	5.02E-13	up	4.053864	ITGAM
206244_at	6.06E-12	up	6.759067	CR1
208783_s_at	0.004769	up	2.21095	CD46
209906_at	7.48E-09	up	4.336492	C3AR1
210184_at	1.17E-06	up	2.086657	ITGAX
212463_at	2.34E-09	up	2.845059	CD59
217552_x_at	5.04E-10	up	3.57143	CR1
218232_at	1.52E-08	up	3.972673	C1QA
218983_at	7.83E-08	up	2.636687	C1RL
220088_at	9.13E-08	up	2.491036	C5AR1
202910_s_at	3.42E-07	up	2.255245	CD97

Table 15. NO/ NADPH oxidase

Probe ID	Pvalue	Arrow	Fold	Gene
201940_at	9.58E-11	up	5.886338	CPD
201941_at	1.14E-09	up	5.264568	CPD
201942_s_at	6.35E-08	up	3.362135	CPD
201943_s_at	7.91E-12	up	6.937615	CPD
204961_s_at	7.26E-08	up	2.016737	NCF1/1B/1C
207677_s_at	5.88E-10	up	2.661943	NCF4
214084_x_at	1.31E-08	up	2.251172	NCF1C

Table 16. MMP

Probe ID	Pvalue	Arrow	Fold	Gene
203167_at	1.02E-13	up	3.135463	TIMP2
203936_s_at	2.89E-16	up	10.59129	MMP9
206871_at	1.04E-06	up	5.3948	ELANE
207329_at	3.41E-11	up	32.06008	MMP8
207890_s_at	1.30E-11	up	3.108211	MMP25
202833_s_at	2.83E-09	up	2.778271	SERPINA1
204614_at	5.64E-08	up	3.074429	SERPINB2
212268_at	8.64E-11	up	5.643009	SERPINB1
213572_s_at	7.52E-11	up	5.130388	SERPINB1

Table 17. Caspase

Probe ID	Pvalue	Arrow	Fold	Gene
202763_at	1.22E-06	up	2.523658	CASP3
204780_s_at	1.71E-04	up	2.524168	FAS
207500_at	4.39E-06	up	2.385929	CASP5
208485_x_at	1.73E-08	down	2.568559	CFLAR
209508_x_at	1.14E-10	down	2.749778	CFLAR
210564_x_at	1.77E-07	down	2.357083	CFLAR
210907_s_at	7.22E-06	up	2.816621	PDCD10
211316_x_at	3.60E-13	down	3.914512	CFLAR
211317_s_at	1.10E-07	down	2.657199	CFLAR
211367_s_at	7.39E-06	up	2.2941	CASP1
211862_x_at	3.34E-08	down	2.575973	CFLAR
213596_at	4.92E-09	up	3.013394	CASP4
214486_x_at	3.71E-08	down	2.177017	CFLAR
215719_x_at	2.24E-06	up	3.678086	FAS
221601_s_at	1.49E-09	down	4.178467	FAIM3
221602_s_at	2.73E-12	down	3.899111	FAIM3

Table 18. Fc receptor

Probe ID	Pvalue	Arrow	Fold	Gene
203561_at	6.67E-09	up	2.023942	FCGR2A
204232_at	8.21E-11	up	2.713677	FCER1G
207674_at	8.78E-08	up	6.420722	FCAR
210992_x_at	1.24E-07	up	2.313229	FCGR2C
211307_s_at	8.29E-08	up	4.563443	FCAR
211395_x_at	1.20E-06	up	2.139768	FCGR2C
211734_s_at	3.84E-05	down	3.85882	FCER1A
211816_x_at	3.58E-05	up	2.405171	FCAR
214511_x_at	2.07E-05	up	3.075548	FCGR1B
216950_s_at	5.51E-08	up	5.08392	FCGR1A/1C

Table 19. CD molecule

Probe ID	Pvalue	Arrow	Fold	Gene
200663_at	7.97E-10	up	2.446524	CD63
201005_at	4.83E-08	up	4.230153	CD9
202351_at	5.59E-10	up	3.163429	ITGAV
202638_s_at	7.74E-08	up	2.891012	ICAM1
202878_s_at	8.07E-06	up	2.265542	CD93
202910_s_at	3.42E-07	up	2.255245	CD97
203645_s_at	2.02E-09	up	9.129274	CD163
204306_s_at	2.48E-06	up	2.098005	CD151
204489_s_at	2.80E-09	up	2.832196	CD44
204490_s_at	3.30E-09	up	2.773283	CD44
204661_at	2.08E-04	down	2.102266	CD52
205173_x_at	8.14E-08	up	3.565981	CD58
205789_at	6.34E-06	up	3.14233	CD1D
205831_at	4.40E-10	down	3.924635	CD2
205988_at	3.64E-19	down	5.606748	CD84
206488_s_at	1.04E-04	up	2.926877	CD36
206761_at	5.72E-06	down	2.026305	CD96
208405_s_at	5.16E-06	up	2.167749	CD164
208650_s_at	7.29E-08	up	4.591438	CD24
208651_x_at	5.17E-10	up	3.761404	CD24
208653_s_at	1.98E-11	up	4.511797	CD164
208654_s_at	3.10E-07	up	5.153189	CD164
209555_s_at	2.87E-05	up	3.18128	CD36
209771_x_at	1.91E-08	up	4.956121	CD24
209835_x_at	3.82E-07	up	2.377499	CD44
210031_at	4.04E-09	down	3.14224	CD247
211744_s_at	7.96E-09	up	3.998247	CD58
211900_x_at	3.47E-14	down	2.437045	CD6
211945_s_at	2.07E-06	up	2.577267	ITGB1
212014_x_at	4.13E-07	up	2.48835	CD44
212063_at	5.59E-07	up	2.205469	CD44
213958_at	2.29E-08	down	2.119745	CD6
215049_x_at	6.80E-09	up	8.964883	CD163
216233_at	3.21E-06	up	4.34145	CD163
216379_x_at	6.81E-09	up	5.765379	CD24
216942_s_at	4.88E-06	up	3.031317	CD58

217523_at	4.41E-13	down	6.665958 CD44
219669_at	1.40E-13	up	34.68958 CD177
222061_at	6.85E-09	up	3.64802 CD58
222292_at	7.05E-11	down	2.150798 CD40
266_s_at	1.78E-10	up	6.956197 CD24

Table 20. Coagulation

Probe ID	Pvalue	Arrow	Fold	Gene
203305_at	2.16E-04	up	2.180403	F13A1
204714_s_at	1.87E-08	up	3.933558	F5
205756_s_at	2.79E-05	up	2.08411	F8
205871_at	7.54E-07	down	3.123419	PLGLA/B1/B2
206655_s_at	2.25E-08	up	5.369561	GP1BB/SEPT5
207808_s_at	6.30E-08	up	2.883896	PROS1
210845_s_at	2.55E-07	up	2.502571	PLAUR
211924_s_at	5.53E-07	up	2.325629	PLAUR
212245_at	6.18E-07	up	2.301938	MCFD2
213258_at	1.07E-06	up	2.352817	TFPI
213506_at	0.002877	up	2.349815	F2RL1
214415_at	1.30E-09	down	5.536361	PLGLB1/B2
214866_at	5.37E-10	up	2.031086	PLAUR
216956_s_at	4.64E-05	up	2.39087	ITGA2B
218718_at	2.79E-10	up	9.385749	PDGFC
204627_s_at	1.30E-06	up	4.180416	ITGB3
203887_s_at	8.66E-09	up	4.530585	THBD
203888_at	4.42E-08	up	2.810682	THBD

Table 21. Glycolysis

Probe ID	Pvalue	Arrow	Fold	Gene
200650_s_at	2.02E-09	up	2.710678	LDHA
200737_at	2.94E-11	up	3.17309	PGK1
201030_x_at	9.45E-05	down	2.016562	LDHB
201251_at	2.51E-10	up	2.67251	PKM2
202464_s_at	6.45E-09	up	7.300454	PFKFB3
202934_at	9.80E-14	up	4.768903	HK2
202990_at	2.15E-12	up	4.196534	PYGL
203502_at	1.24E-04	up	3.670577	BPGM
205936_s_at	5.17E-12	up	4.987516	HK3
206348_s_at	9.53E-11	up	2.597892	PDK3
208308_s_at	3.92E-09	up	2.215685	GPI
209992_at	3.99E-09	up	11.77066	PFKFB2
213453_x_at	2.13E-12	up	2.175151	GAPDH
217294_s_at	3.28E-06	up	2.62132	ENO1
217356_s_at	4.20E-08	up	2.028929	PGK1
218273_s_at	1.01E-07	down	2.250674	PDP1

Table 22. H-ATPase

Probe ID	Pvalue	Arrow	Fold	Gene
200078_s_at	6.15E-13	up	2.530917	ATP6V0B
201171_at	4.49E-10	up	2.484021	ATP6V0E1
201443_s_at	5.84E-06	up	2.32877	ATP6AP2
201971_s_at	4.45E-13	down	5.207561	ATP6V1A
202872_at	1.95E-10	up	6.183733	ATP6V1C1
202874_s_at	6.99E-10	up	5.718367	ATP6V1C1
204158_s_at	5.14E-08	up	2.068726	TCIRG1
208898_at	2.66E-09	up	2.413653	ATP6V1D
213587_s_at	1.13E-08	down	2.067119	ATP6V0E2
206208_at	1.00E-11	up	3.51149	CA4
206209_s_at	4.18E-15	up	7.982899	CA4
209301_at	2.78E-06	up	3.422036	CA2
212536_at	4.38E-09	up	4.21056	ATP11B
213582_at	1.89E-08	up	2.241957	ATP11A

Table 23. Vasodilator

Probe ID	Pvalue	Arrow	Fold	Gene
201494_at	1.01E-08	up	2.190291	PRCP
202912_at	1.20E-08	up	4.330455	ADM
212741_at	0.004196	up	2.027247	MAOA

Table 24. NK cell

Probe ID	Pvalue	Arrow	Fold	Gene
202379_s_at	2.01E-30	down	26.43984	NKTR
205821_at	1.39E-12	down	3.985353	KLRK1
207509_s_at	7.71E-10	down	2.948439	LAIR2
207795_s_at	1.01E-09	down	3.216148	KLRD1
210288_at	1.62E-11	down	5.382525	KLRG1
210606_x_at	1.91E-09	down	3.341239	KLRD1
214470_at	1.11E-04	down	2.103258	KLRB1
215338_s_at	1.06E-24	down	14.54682	NKTR
220646_s_at	1.34E-04	down	2.386466	KLRF1
205488_at	1.01E-05	down	2.867692	GZMA
206666_at	1.84E-07	down	3.446082	GZMK
207460_at	3.78E-09	down	2.502287	GZMM
210164_at	8.91E-09	down	3.75597	GZMB
210321_at	8.94E-10	down	5.800327	GZMH
214617_at	2.22E-06	down	2.646147	PRF1

Table 25. T cell

Probe ID	Pvalue	Arrow	Fold	Gene
205039_s_at	2.79E-08	down	2.22558	IKZF1
205255_x_at	3.09E-08	down	2.955244	TCF7
205456_at	5.31E-08	down	2.877146	CD3E
205488_at	1.01E-05	down	2.867692	GZMA
205495_s_at	5.33E-10	down	4.378694	GNLY
205758_at	1.20E-07	down	3.258815	CD8A
206666_at	1.84E-07	down	3.446082	GZMK
206804_at	1.10E-15	down	5.118528	CD3G
207460_at	3.78E-09	down	2.502287	GZMM
208003_s_at	5.52E-18	down	12.03963	NFAT5
209670_at	5.21E-06	down	2.475029	TRAC
209671_x_at	3.58E-08	down	2.774547	TRAC
209813_x_at	1.49E-09	down	4.424708	TARP
210164_at	8.91E-09	down	3.75597	GZMB
210321_at	8.94E-10	down	5.800327	GZMH
210370_s_at	1.34E-07	down	2.482685	LY9
210555_s_at	1.02E-07	down	2.476832	NFATC3
210556_at	4.68E-08	down	2.850907	NFATC3
210915_x_at	6.23E-06	down	2.847533	TRBC1
210972_x_at	1.78E-07	down	2.875805	TRAC/J17/V20
211144_x_at	5.76E-08	down	3.696107	TARP/TRGC2
211796_s_at	6.35E-06	down	2.926207	TRBC1/C2
211902_x_at	8.99E-07	down	2.286838	TRD@
212759_s_at	3.98E-16	down	3.926594	TCF7L2
212762_s_at	2.70E-09	down	2.376013	TCF7L2
212808_at	1.21E-21	down	5.549449	NFATC2IP
213193_x_at	2.53E-06	down	2.918569	TRBC1
213539_at	1.00E-08	down	3.193378	CD3D
213830_at	5.93E-08	down	3.51036	TRD@
214617_at	2.22E-06	down	2.646147	PRF1
215092_s_at	1.36E-09	down	2.475134	NFAT5
215806_x_at	1.02E-08	down	4.078028	TARP/TRGC2
216191_s_at	4.71E-07	down	4.762182	TRDV3
216920_s_at	2.28E-10	down	5.341667	TARP/TRGC2
217143_s_at	1.26E-08	down	6.055404	TRD@
217526_at	1.43E-12	down	3.846013	NFATC2IP

217527_s_at	2.12E-13	down	5.801224	NFATC2IP
220684_at	7.39E-09	down	2.077709	TBX21
220704_at	2.15E-10	down	5.686157	IKZF1
37145_at	9.67E-10	down	4.340701	GNLY
214032_at	6.60E-08	down	2.523588	ZAP70
204890_s_at	1.65E-07	down	2.638662	LCK
204891_s_at	4.58E-08	down	3.313788	LCK
205831_at	4.40E-10	down	3.924635	CD2
201565_s_at	8.13E-13	down	4.167651	ID2
213931_at	7.33E-08	down	3.546731	ID2/2B

Table 26. B cell

Probe ID	Pvalue	Arrow	Fold	Gene
221969_at	9.96E-13	down	4.199424	PAX5
203140_at	3.09E-10	up	3.687249	BCL6
210105_s_at	9.37E-10	down	3.319013	FYN
210754_s_at	2.98E-10	down	3.545109	LYN
205039_s_at	2.79E-08	down	2.22558	IKZF1
211430_s_at	0.015735	up	2.830679	IGHG1/G2
211643_x_at	0.024398	up	2.10616	IGK
212592_at	0.017267	up	2.569312	IGJ
212827_at	0.008027	down	2.240154	IGHM
214677_x_at	0.031357	up	2.035694	IGLV1-44
214768_x_at	0.006798	up	2.374888	IGKV1-5
217022_s_at	5.28E-05	up	5.197489	IGHA1 /A2
210970_s_at	2.98E-06	up	2.298244	IBTK
217620_s_at	4.31E-12	down	2.785986	PIK3CB
221756_at	5.52E-10	down	2.616271	PIK3IP1
204053_x_at	1.57E-06	up	2.560581	PTEN
204054_at	2.56E-10	up	5.50691	PTEN
211711_s_at	2.54E-08	up	4.673204	PTEN
206370_at	2.95E-09	down	2.443374	PIK3CG
212240_s_at	4.29E-13	down	4.50699	PIK3R1
212249_at	1.96E-06	down	2.560644	PIK3R1