

Progerin impairs vascular smooth muscle cell growth  
via the DNA damage response pathway

(プロジェリンは DNA 損傷応答経路を介して  
血管平滑筋細胞の増殖を障害する)

千葉大学大学院医学薬学府  
先端医学薬学専攻  
(主任：岩間厚志教授)  
木下 大輔

## **Abstract**

Mutations of the lamin A gene cause various premature aging syndromes, including Hutchinson-Gilford progeria syndrome (HGPS) and atypical Werner syndrome. In HGPS (but not atypical Werner syndrome), the cardiovascular system is severely affected, and extensive loss of vascular smooth muscle cells leads to myocardial infarction with premature death. The molecular mechanisms by which lamin A mutations can cause such different premature aging phenotypes as HPGS and atypical Werner syndrome are largely unknown. We performed an interactome analysis using mutant forms of lamin A involved in progeroid syndromes. We found that the mutant lamin A responsible for HGPS, known as progerin, could not interact with proteins related to the DNA damage response, including DNA-dependent protein kinase (DNA-PK), unlike wild-type lamin A or lamin A mutants causing atypical Werner syndrome. We also found that forced expression of progerin in vascular smooth muscle cells led to activation of DNA-PK and cellular growth arrest, while knockdown of DNA-PK attenuated progerin-induced growth arrest. Deletion of p53 also improved the inhibition of cell growth due to forced expression of progerin. These findings suggested that progerin affects the DNA damage response pathway and that dysregulation of this pathway may be responsible for the development of cardiovascular pathology in patients with HGPS.

**Keywords:** cellular senescence, HGPS, DNA-PK, vascular smooth muscle cells, p53

## Introduction

Hutchinson-Gilford progeria syndrome (HGPS) is among the most severe of the premature aging disorders and patients with HGPS die of cardiovascular complications at an average age of only 13 years<sup>1, 2</sup>. While lifestyle-related atherosclerosis involves vascular endothelial cell dysfunction, endothelial cell function is normal in HGPS patients<sup>1</sup>. Instead, they show loss of vascular smooth muscle cells (VSMCs) from the arterial media, which causes maladaptive vascular remodeling and leads to myocardial infarction<sup>1</sup>.

Lamin A is a component of the nuclear lamina, which lies on the inner surface of the nucleus, and it is involved in regulating multiple cellular functions such as maintenance of nuclear integrity, organization of chromatin, DNA replication, and transcription<sup>3, 4</sup>. Lamin A is encoded by the *LMNA* gene and mutations of this gene cause several diseases that affect specific types of mesenchymal cells such as muscle, white adipose tissue, and bone<sup>3, 4</sup>. Other *LMNA* mutations cause premature aging syndromes. The majority of HGPS patients have the G608G mutation that affects splicing in exon 11 to generate a truncated form of lamin A protein called progerin<sup>3, 4</sup>. In contrast, a subset of patients with Werner syndrome, a much less severe form of progeria with a median lifespan of 54 years<sup>5</sup>, have missense mutations such as R133L and L140R<sup>3, 4</sup>.

Several studies using mouse models or cells derived from progeria patients have suggested that DNA damage response pathways may be involved in the pathophysiology of HGPS. In *Zmpste24*<sup>-/-</sup> mice that have similar phenotypic features to HGPS, the downstream targets of p53 were up-regulated and p53 deletion partially reversed some of the markers of premature aging including a shortened lifespan<sup>6</sup>. Phosphorylated histone H2AX is a marker of the response to DNA double-strand breaks, and it was found to be increased in these mice as well as in fibroblasts from HGPS patients<sup>6, 7</sup>. Ataxia telangiectasia mutated (ATM) is a kinase that is rapidly and

specifically activated in response to DNA double-strand breaks, and it was found to be activated in *Zmpste24*<sup>-/-</sup> mice as well as in *Lmna* G609G/G609G mice that produce progerin and display clinical features of HGPS<sup>8</sup>. Changes in the localization and expression of DNA-dependent protein kinase (DNA-PK), another DNA damage response kinase, have been reported in HGPS fibroblasts, although the role of DNA-PK in HGPS is not clear<sup>9</sup>. Studies using induced pluripotent stem cells obtained from HGPS patients have detected cell type-specific toxicity of progerin for VSMCs<sup>9, 10</sup>, reflecting the unique pattern of arteriosclerosis in HGPS.

While there has been an increase in our knowledge of these syndromes, important questions remain unanswered. For example, “why do mutations of the same gene lead to such different premature aging phenotypes as HGPS and atypical Werner syndrome?”, “what causes cell-specific toxicity of progerin for cells with a mesenchymal origin?”, and “how are DNA damage response pathways related to the etiology of HGPS?”. In the present study, we attempted to address these issues by performing comparative interactome analysis of mutant forms of lamin A involved in HGPS and atypical Werner syndrome.

## **Results**

### **Interactome analysis of wild-type and mutant lamin A**

In order to understand how mutation of lamin A causes more severe premature aging than other mutations in HGPS, we transfected HEK293 cells with four types of flag-tagged lamin A as the bait and performed immunoprecipitation of cell lysates with an anti-flag antibody, after which binding proteins were subjected to LC-MS/MS analysis. The baits were flag-tagged wild-type lamin A, flag-tagged lamin A R133L (a mutant causing atypical Werner Syndrome), flag-tagged lamin A L140R (another mutant causing atypical Werner Syndrome), and flag-tagged progerin (Figure 1). We identified 55 binding partners of wild-type lamin A, which included some proteins previously

reported to interact with lamin A, validating the quality of the present experiments (Table 2). The three lamin A mutants retained the ability to interact with some of the proteins that bound to wild-type lamin A, but most were no longer recognized. L140R was unable to bind with 30 of the 55 proteins, while R133L lost the ability to bind to 32 proteins and progerin could not bind to 43 proteins (Figure 2 and Table 3). We also found that the lamin A mutants could interact with a substantial number of proteins to which wild-type lamin A could not bind (Figure 2 and Table 3). According to interactome analysis, progerin showed the largest loss and smallest gain in the number of protein-protein interactions compared with wild-type lamin A. These results led us to hypothesize that the normal lamin A protein network is most severely affected in HGPS among the laminopathies associated with premature aging and that alterations of protein interactions may contribute to the characteristic phenotypic features of this disease.

Next, we performed gene ontology (GO) analyses in order to detect functional differences between progerin-associated proteins. Using the functional annotation tool DAVID, we searched for GO terms concentrated in the sets of proteins interacting with wild-type lamin A, R133L, L140R, or progerin. Because several GO terms with similar functions showed almost complete overlap, we manually categorized them into common biological terms (Table 1). We found seven terms that were significantly enriched in wild-type lamin A-bound proteins (Table 1). Interestingly, proteins that interacted with any lamin A mutant causing atypical Werner syndrome usually shared almost all of these terms, although the interacting molecules did not correspond exactly to wild-type lamin A (Table 1 and Table 3). It is noteworthy that progerin lacked two terms when compared with the other three proteins, which were “DNA damage response” and “muscle” (Table 1). These data suggest that progerin has lost a set of interaction partners with specific functions rather than losing the ability to bind to proteins randomly.

### **Lack of progerin/DNA-PK interaction is associated with activation of DNA-PK**

We assigned the three GO terms “DNA-dependent protein kinase (DNA-PK)–DNA ligase 4 complex”, “non-homologous end joining complex”, and “replication fork” to the category of DNA damage response (Table 1). DNA-PKcs is the catalytic subunit of DNA-PK, a nuclear DNA-dependent serine/threonine protein kinase.<sup>11</sup> DNA-PKcs is required for the non-homologous end joining (NHEJ) DNA repair pathway, which repairs double-strand breaks in DNA. We focused on the term “DNA-dependent protein kinase–DNA ligase 4 complex” because DNA-PKcs and its binding partners Ku80 and Ku70 were all detected in the interactomes of wild-type lamin A, R133L, and L140R, while none of them were detected among the progerin-associated proteins (Table 3).

Many proteins have been identified as substrates for the kinase activity of DNA-PK. Autophosphorylation of DNA-PKcs appears to play a key role in NHEJ and is thought to induce a conformational change that allows end-processing enzymes to access the ends of the double-strand break. In addition, DNA-PKcs has been reported to interact with a number of regulators of DNA metabolism. To investigate the interaction between progerin and DNA-PKcs, we transfected cells with flag-tagged lamin A or flag-tagged progerin and then performed immunoprecipitation with an anti-flag antibody and western blot analysis for DNA-PKcs expression. DNA-PKcs was easily detected when cells were transfected with flag-tagged lamin A, while it was markedly reduced in cells transfected with flag-tagged progerin (Figure 3A), validating the results obtained by mass spectrometry. To examine how lamin A influenced the activation of DNA-PKcs, we further assessed its phosphorylation. While introduction of wild-type lamin A did not affect the phosphorylation of DNA-PKcs, introduction of progerin led to a marked increase of its phosphorylation (Figure 3B). These results suggested that accumulation of progerin could increase the activity of DNA-PK by changing its binding properties.

### **Progerin impairs VSMC growth in a DNA-PK and p53-dependent manner**

Because VSMCs rather than vascular endothelial cells are involved in arteriosclerosis associated with HGPS, we tested the influence of progerin on the growth of VSMCs and human umbilical vein endothelial cells (HUVECs) by using a retroviral vector that encoded wild-type lamin A or progerin. Introduction of progerin into VSMCs strongly reduced cell growth and shortened the replicative lifespan (Figure 4A and B). In contrast, introduction of progerin had no effect on the growth and lifespan of HUVECs (Figure 4C and D), showing a cell type-specific effect of progerin. These results are consistent with the known pathology of HGPS as well as with a previous report about iPS cells<sup>10</sup>.

We next examined whether knockdown of DNA-PKcs with small interfering RNA (siRNA) could improve the growth of VSMCs after introduction of progerin. We found that siRNA targeting DNA-PKcs reduced the DNA-PKcs protein level in cultured VSMCs (Figure 5A). In addition, knockdown of DNA-PKcs reversed the suppression of cell growth by progerin (Figure 5B and C), suggesting that activation of DNA-PK could account for the antiproliferative effect of progerin on VSMCs.

VSMC numbers did not increase when culture was continued for 2 months after introduction of progerin. When we harvested these cells and performed western blot analysis of cell cycle checkpoint proteins related to the DNA damage response and cellular senescence, we found that expression of p53, p21, and p16 was increased by introduction of progerin compared with wild-type lamin A (Figure 6A). It is well known that DNA-PK cooperates with ATM, leading to phosphorylation and activation of p53<sup>12, 13</sup>. Accordingly, we speculated that progerin-induced activation of DNA-PK might up-regulate p53 activity, thereby inducing cell growth arrest. To test this hypothesis, we introduced siRNA targeting p53 into progerin-infected VSMCs and found that this siRNA counteracted the anti-proliferative effect of progerin on VSMC growth (Figure 6B and C). These results suggested that progerin suppresses VSMC growth via activation of the DNA damage response pathway.

### **Progerin upregulates pro-inflammatory gene expression in a NF- $\kappa$ B-dependent, but DNA-PK-independent, manner**

Accumulation of prelamin A isoforms at the nuclear lamina was reported to trigger activation of NF- $\kappa$ B and secretion of high levels of pro-inflammatory cytokines in two different mouse models of HGPS<sup>8</sup>. We investigated whether progerin overexpression in VSMCs upregulated pro-inflammatory molecules via a DNA-PK dependent pathway. Microarray analysis revealed upregulation of the production of pro-inflammatory cytokines and extracellular proteases (including MMP-3, GM-CSF, and IL-8) by VSMCs after introduction of progerin compared with wild-type lamin A (Table 4). Upregulation of these molecules was also confirmed by real-time PCR (Figure 7). Inhibition of NF- $\kappa$ B signaling by siRNA targeting *RELA* (p65) attenuated the progerin-induced upregulation of GM-CSF and IL-8, while MMP-3 expression was not significantly affected (Figure 7). We next tested three siRNAs targeting DNA-PKcs or ATM, but none of them downregulated the expression of these pro-inflammatory molecules (Figure 7 and data not shown), suggesting that progerin-induced inflammatory gene activation is independent of DNA-PK activation.

### **Discussion**

In the present study, we performed affinity purification using wild-type lamin A and three mutant forms of lamin A associated with premature aging syndromes as the bait, employing mass spectrometry for analysis of the samples. As a result, we identified over 50 proteins that had not been previously recognized as binding to lamin A. We found that part of this protein network was shared between wild-type lamin A and the lamin A mutants that cause atypical Werner syndrome, although more than half of these proteins did not interact with the mutants. In addition, only a few of the proteins bound to progerin, suggesting that the mutation underlying HGPS most severely impairs the ability of lamin A to interact with functional proteins. Consistent with this concept, our



GO functional analysis revealed that progerin did not interact with a set of proteins that had functions categorized into “DNA damage response” and “muscle”, while the two lamin A mutants causing atypical Werner syndrome still interacted with proteins related to the “DNA damage response”. Since about 25% of lamin A-binding proteins fitted into this category, we focused on the DNA damage response. Among DNA-PKcs and its associated proteins, Ku80 and Ku70 were found to interact with wild-type lamin A and the two mutants causing atypical Werner syndrome, but not with progerin. We also demonstrated that overexpression of progerin upregulated DNA-PKcs phosphorylation in VSMCs and induced premature senescence of these cells, while DNA-PK knockdown reversed progerin-induced cell growth arrest. These results suggested that reduced binding of progerin to various proteins interferes with the DNA damage response, leading to the development of vascular pathology in HGPS.

While data from several mouse models of HGPS have suggested the importance of the DNA damage response,<sup>6, 8, 9</sup> the actual role of this pathway remains unclear. Osorio et al. reported that accumulation of progerin triggers a signaling pathway involving ATM that activates NF- $\kappa$ B,<sup>8</sup> and they also demonstrated that NF- $\kappa$ B-driven inflammation is responsible for several important features of the progeroid phenotypes. Interestingly, inhibition of the NF- $\kappa$ B pathway by genetic or pharmacological strategies was able to prevent these phenotypic alterations, demonstrating the causal role of this inflammatory pathway in the pathogenesis of accelerated aging. In agreement with their results, we showed that introduction of progerin into VSMCs led to upregulation of pro-inflammatory genes, while inhibition of NF- $\kappa$ B signaling attenuated the inflammatory response induced by progerin. However, inhibition of ATM or DNA-PK failed to inhibit progerin-induced upregulation of pro-inflammatory genes in VSMCs, suggesting progerin induces inflammation via a mechanism that is independent of the DNA damage response.

Signaling kinases (ATM, ATR and, DNA-PK) are recruited to sites of DNA

damage and are activated at these sites, leading to the local assembly of checkpoint and DNA repair factors and promoting the phosphorylation of transducer kinases (Chk1 and Chk2), which converge on p53<sup>14</sup>. Marked upregulation of p53 target genes has been reported in a mouse model of HGPS, while blocking the activation of p53 attenuates premature aging<sup>6</sup>. In aged HGPS cells, Liu et al. found an increase of phosphorylated Chk1 and Chk2 owing to the activation of ATM and ATR<sup>15</sup>. Phosphorylated p53 was also increased, demonstrating that the ATR and ATM checkpoints were persistently activated, as also confirmed by other researchers<sup>16-18</sup>. In the present study, we demonstrated that accumulation of progerin leads to activation of DNA-PK and plays a causal role in senescence of VSMCs, providing evidence that DNA-PK could contribute to the pathogenesis of HGPS.

Various explanations have been proposed for the cell type-specific pathology of laminopathies, including progerin-mediated exhaustion of stem cell pools<sup>19</sup>, defects of mesenchymal lineage differentiation<sup>20</sup>, impairment of the DNA damage repair response<sup>21</sup>, and nuclear fragility in mechanically stressed cells such as cardiomyocytes<sup>22</sup>. Recently, Liu et al. generated induced pluripotent stem cells (iPSCs) from the fibroblasts of patients with HGPS. They elegantly demonstrated that progerin expression and associated premature senescence were markedly suppressed in the pluripotent state, while the aging phenotype emerged along with progerin expression after differentiation of the cells into VSMCs. However, this does not occur when HGPS-iPSCs undergo differentiation into fibroblasts<sup>9</sup>. Zhang et al. also generated HGPS-iPSCs and found that progerin levels were highest in mesenchymal stem cells (MSCs) and VSMCs differentiated from the pluripotent cells<sup>10</sup>. Because these cells were sensitive to various stresses, they speculated that progeria may be related to a shortage of MSCs needed for tissue repair. In the present study, we observed that forced expression of progerin induced premature senescence of VSMCs, but not endothelial cells, although the mechanisms underlying these observations are still obscure.

In conclusion, our findings suggest that progerin inhibits VSMC growth via the DNA damage response pathway and that this pathway probably contributes to the pathogenesis of HGPS. Further interactome analysis of lamin A mutants involved in premature aging syndromes could provide a platform for future studies on the link between lamin A and premature aging.

## **Materials and Methods**

### **Cell culture**

HEK293 cells were cultured in DMEM (Sigma) supplemented with 10% FBS, streptomycin ( $0.1 \mu\text{g ml}^{-1}$ ), and penicillin G ( $100 \text{ units ml}^{-1}$ ). Human VSMCs and HUVECs were purchased from Lonza and cultured according to the manufacturer's instructions. Culture was done at  $37^{\circ}\text{C}$  in a humidified incubator with 5%  $\text{CO}_2$  and proliferation was assessed by counting cells after subculture. We defined senescent cells as those that did not increase in number and remained subconfluent after 2 weeks of culture. The number of population doublings (PD) was calculated as follows:  $\text{PD} = \log(\text{number of cells after culture}/\text{initial number of cells})/\log 2$ .

### **Transfection of expression vectors and retroviral infection**

The expression vector pcDNA<sup>TM</sup>5/FRT/TO (Invitrogen) was cut with *Bam* H I and *Xho* I. Fragments of lamin A , progerin, lamin A R133L, or lamin A L140R were ligated into the corresponding restriction sites of pcDNA<sup>TM</sup>5/FRT/TO. The resulting expression vectors were transfected into HEK293 cells by using Fugene. We created vectors based on pLNCX2 (Clontech, Palo Alto, CA, USA) that expressed wild-type lamin A or progerin for retroviral infection, which was done as described previously<sup>23</sup>. Briefly, VSMCs or HUVECs (passages 4–6) were plated at  $5 \times 10^5$  cells in 100-mm dishes at 24 hours before infection. Then the culture medium was replaced by retroviral stock medium supplemented with  $8 \mu\text{g ml}^{-1}$  polybrene (Sigma). From 48 hours after infection, the cells were selected by culture for 7 days in  $500 \mu\text{g ml}^{-1}$  G418. After selection,  $2 \times 10^5$  cells were seeded in 100-mm dishes on the 8th day post-infection, which was designated as day 0. The respective empty vectors were used as controls. In some experiments, after retroviral infection had been performed, siRNAs purchased from Ambion or Invitrogen were transfected at  $10 \text{ nmol l}^{-1}$  with RNAiFect (Qiagen) or Lipofectamine RNAiMAX (Invitrogen) according to the instructions of the respective

manufacturers.

### **Western blot analysis**

Whole-cell lysates were prepared in lysis buffer (10 mM Tris-HCl, pH 8, 140 mM NaCl, 5 mM EDTA, 0.025% NaN<sub>3</sub>, 1% Triton X-100, 1% deoxycholate, 0.1% SDS, 1 mM PMSF, 5 µg ml<sup>-1</sup> leupeptin, 2 µg ml<sup>-1</sup> aprotinin, 50 mM NaF, and 1 mM Na<sub>2</sub>VO<sub>3</sub>). The lysates (40–50 µg) were resolved by SDS-PAGE and proteins were transferred to a PVDF membrane (Millipore), which was incubated with the primary antibody followed by anti-rabbit or anti-mouse immunoglobulin-G conjugated with horseradish peroxidase (Jackson). Specific proteins were detected by the enhanced chemiluminescence method (Amersham). The primary antibodies used for western blotting were as follows: anti-p53 antibody (#2524), anti-actin antibody (#4967) (Cell Signaling), and anti-GAPDH antibody (sc-20357, Santa Cruz), anti-DNA-PK- $\alpha$  antibody (sc-9051, Santa Cruz), anti-phospho-DNA-PK- $\alpha$  antibody (Thr2609) (sc-101664, Santa Cruz), anti-Rabbit Monoclonal Anti-FLAG antibody (F2555, Sigma).

### **Real-time PCR**

Total RNA (1 µg) was isolated from tissue samples with RNA-Bee (Tel-Test Inc.). Real-time PCR (qPCR) was performed by using a Light Cycler 480 (Roche) with the Taqman Universal Probe Library and the Light Cycler 480 Probes Master (Roche) according to the manufacturer's instructions. For quantification of the copy number, we used Light Cycler 480 software (version 1.5, Roche) and employed the 'fit points' method according to the manufacturer's instructions. GAPDH was used to normalize the amount of mRNA in each sample.

### **Transcriptome analysis**

VSMCs with p53 deficiency (overexpressing E6) were infected with retroviral vectors

encoding lamin A or progerin and cells were harvested after 30 days. Then total RNA was isolated with RNA-Bee (Tel-Test, Inc.) and the genetic profile of lamin A and progerin were analyzed by using a Human Gene Expression 4x44K v2 Microarray Kit (Agilent Technologies) (n=4 per group). Raw data were subjected to log<sub>2</sub> transformation and normalized by using GeneSpring GX v7.3.1 (Agilent Technologies). Genes showing differential expression (q<0.05) were determined by BH-FDR. Gene ontology analysis was performed using the Database for Annotation, Visualization and Integrated Discovery (DAVID) v6.7. Finally, the gene expression data thus obtained were deposited in the Gene Expression Omnibus database (GSE47553).

### **Identification of proteins by LC-MS/MS**

Immunoprecipitated protein samples (approximately 100 µl) were mixed with 400 µl of methanol. 100 µl chloroform was mixed with the samples, followed by the addition of 300 µl distilled water and stirred for 2 minutes. After centrifugation at 2,000 rpm for 2 minutes, the supernatant was removed and 300 µl methanol was added. After centrifugation at 15,000 rpm for 5 minutes, the supernatant was removed and the samples were dried with an evaporator. Dried samples were dissolved with the buffer including 180 mg urea, 0.12 M Tris HCl buffer 1.5M Tris HCl (pH 8.8) 33.3 µl, and H<sub>2</sub>O 370 µl, then mixed with 2 µl Tris (2-CarboxyEthyl) Phosphine (TCEP), and incubated at 37 °C for 2 hours. One µl of methyl-methane-thio-sulphonate (MMTS) was added and incubated at room temperature for 10 minutes, followed by overnight incubation with 1 µl lysyl endopeptidase. Digested samples were dried with an evaporator, and then dissolved with 200 µl of 2% acetonitrile/0.1% trifluoroacetic acid. The samples were desalted with a tip made with C18 Empore Disk. The tips including samples were added with 100 µl of 70% acetonitrile/0.1% trifluoroacetic acid. Samples were centrifuged at 2,000 rpm for 5 minutes and the flow-through was discarded. 100 µl of 2% acetonitrile/0.1% trifluoroacetic acid was added and centrifuged at 2,000 rpm for

5 minutes. The flow-through was discarded followed by the addition of 200  $\mu$ l of 2% acetonitrile/0.1% trifluoroacetic acid. Each 100  $\mu$ l of samples was added to 2 tips, and was centrifuged at 2,000 rpm for 5 minutes, followed by the discard of the flow-through. The tip was loaded onto a new 1.5 ml tube, 100  $\mu$ l of 2% acetonitrile/0.1% trifluoroacetic acid was added onto the tip, and the tubes were centrifuged. Eluted samples were dried with an evaporator, and dissolved with 12  $\mu$ l of 2% acetonitrile/0.1% formic acid, followed by centrifugation at 15,000 rpm for 5 minutes. The supernatant was used for LC-MS/MS analysis. The data were analyzed using MASCOT software (Matrix Science, Wyndham Place, UK). Biogrid (<http://thebiogrid.org/>) was used to analyze if identified proteins are novel or previously reported. The proteins thus identified were categorized with the Database for Annotation, Visualization and Integrated Discovery (DAVID v6.7).

### **Statistical analysis**

Results are shown as the mean  $\pm$  SEM. The two-tailed Student's *t*-test or one-way ANOVA was used to assess the statistical significance of differences. In all analyses,  $P < 0.05$  was considered significant.

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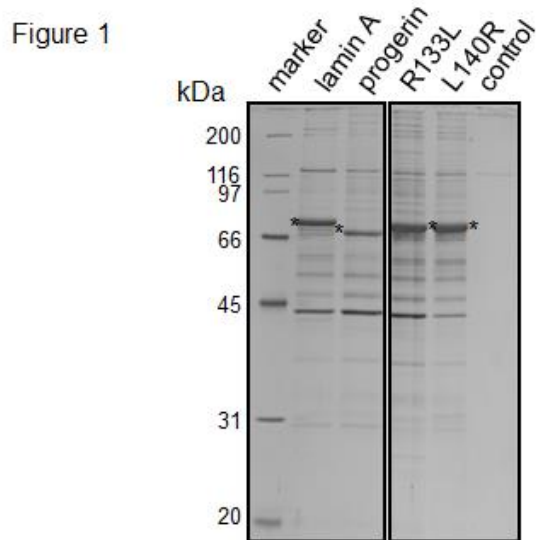
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## Figure legends

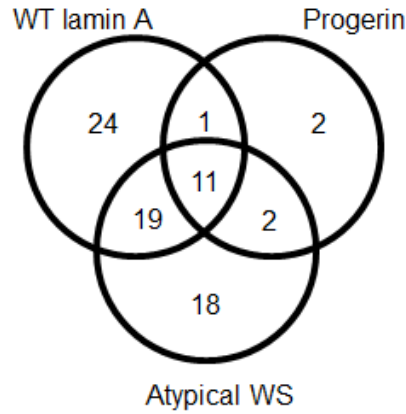
### Figure 1 Isolation of lamin A or lamin A mutants-associated complexes.



Wild-type lamin A or lamin A mutant-associated complexes were isolated by immunoprecipitation from HEK293 cells transfected with lamin A or lamin A mutant expression vectors (progerin, R133L, L140R). The immune-isolated complexes were resolved by SDS-PAGE on a 12.5% gel followed by silver staining. Untransfected HEK 293 cells were used in control experiments (control). Asterisks indicate FLAG-tagged lamin A or lamin A mutants.

**Figure 2 Venn diagram for the interactome analysis**

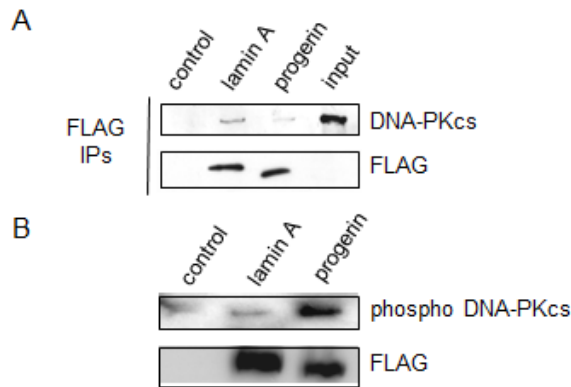
Figure 2



We identified 55 binding partners of wild-type lamin A, but most were not recognized by lamin A mutants, in particular, progerin.

**Figure 3 Progerin loses affinity with DNA-PK and activates it**

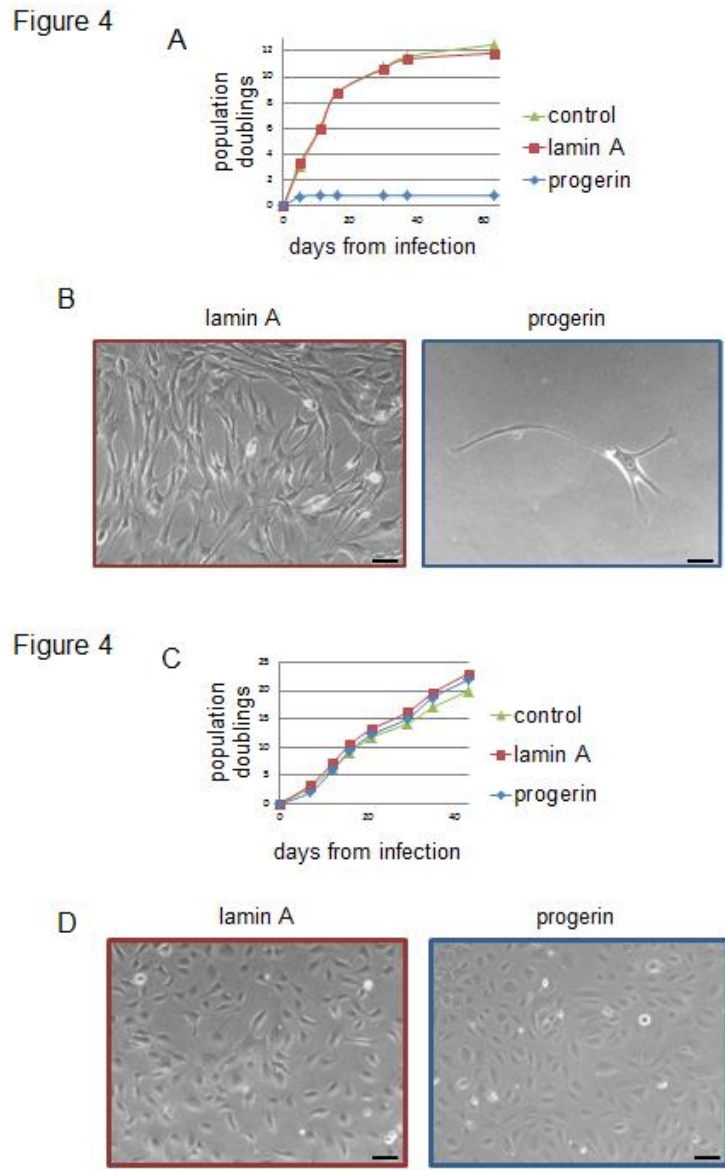
Figure 3



(A) An expression vector encoding flag-tagged wild-type lamin A or progerin was transduced into HEK293 cells, after which co-immunoprecipitation was conducted with anti-flag antibody. Then the samples were subjected to western blot analysis for detection of DNA-PKcs and flag protein. The empty vector was used as a control.

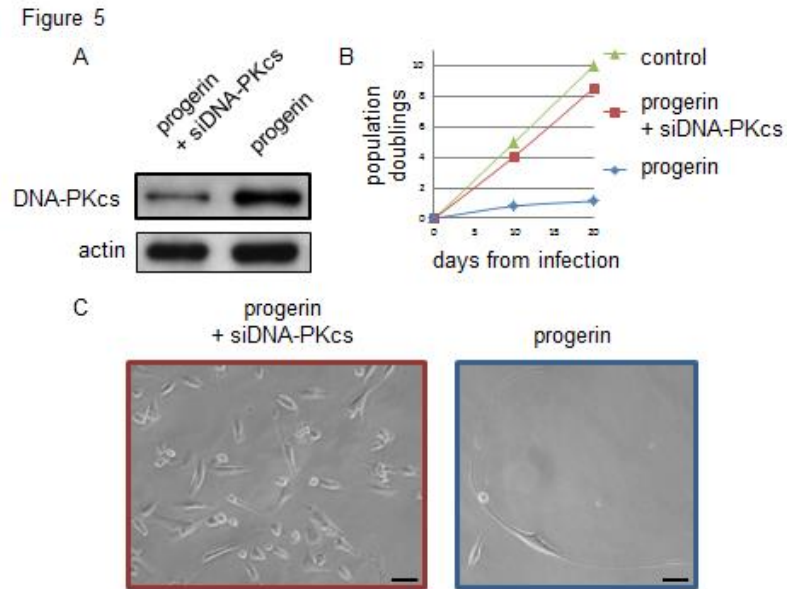
(B) An expression vector encoding flag-tagged wild-type lamin A or progerin was transduced into HEK293 cells, following which the levels of phosphorylated DNA-PKcs and flag protein were examined by western blot analysis.

**Figure 4 Progerin impairs the growth of VSMCs but not HUVECs**



(A) VSMCs were infected with a retroviral vector encoding wild-type lamin A or progerin and population doubling was examined. (B) Representative pictures of VSMCs infected with the wild-type lamin A vector or progerin vector. Scale bar=100  $\mu$ m. (C) HUVECs were infected with a retroviral vector encoding wild-type lamin A or progerin and population doubling was examined. (D) Representative pictures of HUVECs infected with the wild-type lamin A vector or the progerin vector. Scale bar=100  $\mu$ m.

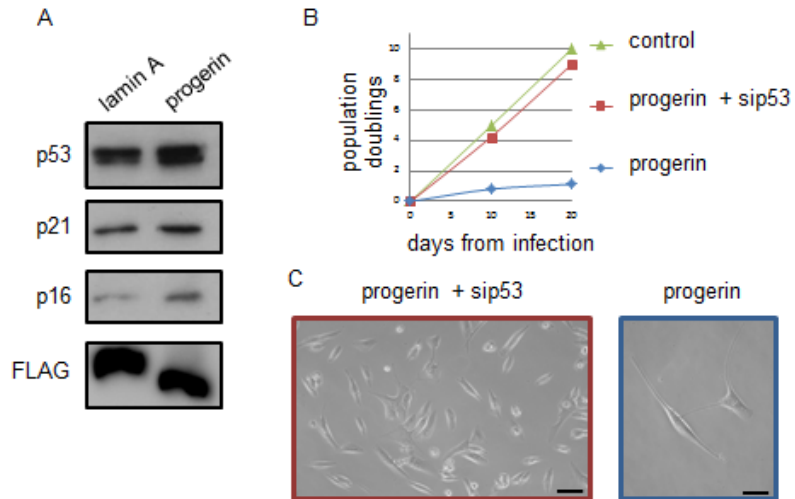
**Figure 5 DNA-PKcs knockdown attenuates progerin-induced inhibition of VSMC growth**



(A) VSMCs were infected with a retroviral vector encoding progerin with or without siRNA targeting DNA-PKcs, after which expression of DNA-PKcs was examined by western blot analysis. (B) Population doubling was examined using VSMCs prepared as explained in (A). (C) Representative pictures of VSMCs prepared as explained in (A). Scale bar=100  $\mu$ m.

## Figure 6 p53 knockdown ameliorates progerin-induced inhibition of VSMC growth

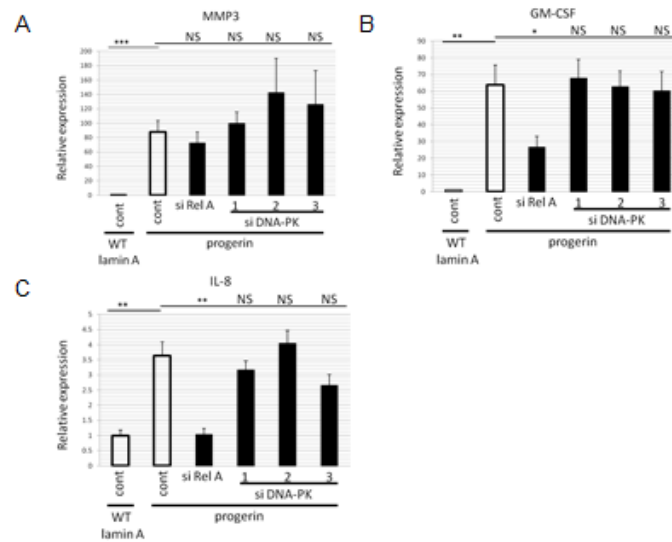
Figure 6



(A) VSMCs were infected with a retroviral vector encoding wild-type lamin A or progerin, following which expression of p53, p21, and p16 was examined by western blot analysis. (B) VSMCs were infected with a retroviral vector encoding progerin with or without siRNA targeting p53, after which population doubling was examined. (C) Representative pictures of VSMCs prepared as explained in (B). Scale bar=100  $\mu$ m.

**Figure 7 Knockdown of RelA, but not DNA-PK, attenuates progerin-induced upregulation of pro-inflammatory molecules in VSMCs**

Figure 7



VSMCs were infected with a retroviral vector encoding wild-type lamin A or progerin and with siRNA targeting the NF- $\kappa$ B component RELA (p65) or DNA-PKcs. Then expression of MMP3, GM-CSF, and IL-8 was examined by real-time PCR. Control siRNA was also transfected as a control. NS, not significant. \*  $P < 0.05$ . \*\*  $P < 0.01$ .

**Table1** : Gene Ontology terms of proteins ineteracted with wild-type lamin A, R133L, L140R, or progerin.

	lamin A	progerin	R133L	L140R
DNAdamage response	●		●	●
Muscle	●			
Cytoskeleton	●	●	●	●
Intranuclear	●	●	●	●
nuclear lamina	●	●	●	●
nuclear membrane	●	●	●	●
nuclear periphery	●	●	●	●

**DNA Damage Response**

DNA-dependent protein kinase-DNA ligase 4 complex, nonhomologous end joining complex

**muscle**

contractile fiber, contractile fiber part, fascia adherens, I band, myofibril, sarcomere, Z disc

**cytoskeleton**

actin cytoskeleton, Arp2/3 protein complex, cortical actin cytoskeleton, cytoskeleton, cytoskeletal part, intermediate filament, intermediate filament cytoskeleton, lamin filament, spectrin

**intranuclear**

chromatin, chromosome, chromosomal part, chromosome telomeric region, DNA replication factor A complex, intracellular organelle lumen, nuclear chromosome, nuclear chromosome part, nuclear chromosome telomeric region, nuclear matrix (p, 133), nuclear replication fork, nuclear replisome, nuclear telomere cap complex, nucleoplasm, nucleoplasm part, replisome, telomere cap complex

**nuclear lamina**

lamin filament (p, 133,140), nuclear lamina

**nuclear membrane**

endomembrane system, membrane-enclosed lumen (133), nuclear inner membrane, nuclear membrane, organelle inner membrane (p,133), organelle membrane, protein-DNA complex

**nuclear periphery**

cell-cell adherens junction (140), cell cortex, cell leading edge, cell projection, envelope, intercalated disc, intracellular non-membrane-bounded organelle, intracellular organelle lumen, lamellipodium, membrane-enclosed lumen, non-membrane-bounded organelle, nuclear envelope, nuclear lumen, nuclear periphery, nuclear pore, organelle envelope, organelle lumen, pore complex,



**Table2 : Binding partners of wild-type lamin A**

1	Accession	sample1	Unused	Total	%Cov	%Cov(50)	%Cov(95)	sample2	Unused	Total	%Cov	%Cov(50)	%Cov(95)
2	P02545 LMNA_HUMAN		102.68	102.68	95.6325	66.41566	64.759		104.83	104.83	96.6867	76.95783	73.3434
3	P20700 LMNB1_HUMAN		36.33	36.33	74.2321	52.21843	43.3447		38.5	38.5	79.5222	61.77474	41.8089
4	Q03252 LMNB2_HUMAN		16.07	16.45	45.1667	29.33333	19.6667		21.3	22.55	54	34.16667	30.8333
5	Q14247 SRC8_HUMAN		13.25	13.25	41.0909	20.90909	14.5455		19.08	19.08	57.2727	27.27273	21.8182
6	Q93009 UBP7_HUMAN		7.13	7.13	21.9601	7.350272	3.0853		18.79	18.79	29.3103	15.33575	14.1561
7	O60684 IMA7_HUMAN		8.51	8.51	27.7985	19.02985	14.5522		14.89	14.89	44.9627	22.94776	21.2687
8	P12956 KU70_HUMAN		8.76	8.76	30.0493	11.98686	10.3448		11.33	11.33	34.1544	15.27094	12.8079
9	P78527 PRKDC_HUMAN								11.25	11.25	16.2064	2.131783	1.91376
10	O75531 BAF_HUMAN		7.31	7.31	65.1685	43.82023	43.8202		10.51	10.51	65.1685	53.93258	43.8202
11	P13010 KUB8_HUMAN		0.91	0.91	16.6667	2.459016	0		9.58	9.58	36.3388	10.79235	10.7924
12	P42167 LAP2B_HUMAN		0	2.32	10.3524	2.643172	2.64317						
13	Q13813 SPTA2_HUMAN								6.04	6.04	21.157	2.022654	2.02265
14	Q96I20 PAWR_HUMAN								6.01	6.01	38.2353	25.88235	25.8824
15	P27694 RFA1_HUMAN		1.04	1.04	10.7143	1.948052	0		6	6	22.4026	9.415584	9.41558
16	P61160 ARP2_HUMAN		3.47	3.47	26.1421	6.598984	3.80711		5.9	5.9	24.3655	11.42132	9.13706
17	P10515 ODP2_HUMAN								5.3	5.3	22.3127	7.491857	7.49186
18	P42166 LAP2A_HUMAN		4.02	4.02	23.7752	4.034582	4.03458		5.15	5.15	23.6311	7.348703	5.33141
19	O15145 ARPC3_HUMAN		2.28	2.28	20.2247	7.303371	7.30337		4.92	4.92	42.6966	29.21348	21.9101
20	Q8TD47 RS4Y2_HUMAN		0	2	23.9544	4.562738	4.56274						
21	O75083 WDR1_HUMAN		1.7	1.7	12.5413	2.970297	0		4.31	4.31	19.802	7.260726	3.9604
22	Q92804 RBP56_HUMAN								0	2	7.93919	1.52027	1.52027
23	O15143 ARC1B_HUMAN		4	4	17.2043	9.408602	9.4086		4	4	15.5914	8.333334	8.33333
24	Q01469 FABPE_HUMAN								3.4	3.4	23.7037	19.25926	19.2593
25	O75131 CPNE3_HUMAN		3.7	3.7	10.987	4.841713	4.84171		2.94	2.94	17.1322	6.89013	2.42086
26	P60903 S10AA_HUMAN								2.68	2.68	26.8041	26.80412	17.5258
27	F52294 IMA1_HUMAN		1.7	3.23	15.2416	4.832714	4.83271		2.6	6.64	24.3494	10.96654	8.92193
28	Q9UNE7 STUB1_HUMAN								2.6	2.6	20.462	12.87129	5.94059
29	P59998 ARPC4_HUMAN		1.3	1.3	8.33333	8.333334	8.33333						
30	P19105 MLRM_HUMAN		0	2	15.2047	7.017544	7.01754		2.22	2.22	20.4678	7.017544	7.01754
31	P61158 ARP3_HUMAN		2	2	2.87081	2.870813	2.87081		2.17	2.17	27.0335	4.066985	4.06699
32	Q92747 ARC1A_HUMAN		0.71	0.71	13.2432	3.243243	0		2.14	2.14	19.1892	3.783784	3.78378
33	Q01082 SPTB2_HUMAN								2.02	2.02	12.4365	1.649746	1.64975
34	Q9Y608 LRRF2_HUMAN								2.02	2.02	18.8627	3.32871	3.32871
35	P63092 GNAS2_HUMAN								2.01	2.01	15.4822	2.791878	2.79188
36	Q96CT7 CC124_HUMAN								2	2	45.7399	5.381166	5.38117
37	O15084 ANR28_HUMAN								2	2	10.8656	0.644567	0.64457
38	P53999 TCP4_HUMAN		2	2	33.0709	10.23622	10.2362		2	2	43.3071	10.23622	10.2362
39	P50402 EMD_HUMAN		2	2	18.1102	3.937008	3.93701		2	2	3.93701	3.937008	3.93701
40	O95816 BAG2_HUMAN		2.31	2.31	18.0095	12.32227	5.21327		1.99	1.99	26.0664	12.32227	5.21327
41	O15144 ARPC2_HUMAN		1.28	1.28	21.3333	3.333334	0		1.9	1.9	35	12	0
42	P08133 ANXA6_HUMAN								1.89	1.89	26.3001	6.686478	0
43	Q9NZ01 GPSN2_HUMAN								1.7	1.7	4.54545	3.246753	3.24675
44	O60673 DPOLZ_HUMAN								1.55	1.55	16.9968	0.479233	0.47923
45	P35244 RFA3_HUMAN								1.52	1.52	14.0496	14.04959	14.0496
46	P52292 IMA2_HUMAN								1.35	1.35	23.8185	3.591682	0
47	Q71D13 H92_HUMAN								1.31	1.31	43.3824	5.882353	5.88235
48	Q7Z7G8 VP13B_HUMAN								1.23	1.23	5.69368	0.323222	0
49	P34931 HS70L_HUMAN								1.15	8.88	39.4696	14.9766	14.9766
50	P29084 T2EB_HUMAN								1	1	41.5808	4.467354	0
51	Q13185 CBX3_HUMAN								0.84	0.84	29.5082	7.650273	0
52	Q8WUQ7 CS029_HUMAN								0.72	0.72	8.98551	1.014493	0
53	P14923 PLAK_HUMAN								0.5	0.5	6.3172	1.612903	0
54	Q14839 CHD4_HUMAN								0.48	0.48	6.74686	0.575314	0
55	P02452 CO1A1_HUMAN								0.47	0.47	8.19672	1.36612	0
56	Q9HAZ2 PRD16_HUMAN								0.47	0.47	3.21317	1.097179	0

**Table3 : binding partners of wild-type and mutant lamin A**

1	Accession	novelty	WT1	WT2	L140R1	L140R2	R133L1	R133L2	progerin1	progerin2
2	P02545 LMNA_HUMAN	bait								
3	P20700 LMNB1_HUMAN	known								
4	Q03252 LMNB2_HUMAN	known								
5	Q14247 SRC8_HUMAN	new								
6	Q93009 UBP7_HUMAN	new								
7	O60684 IMA7_HUMAN	new								
8	P12956 KU70_HUMAN	known								
9	P78527 PRKDC_HUMAN	known								
10	O75531 BAF_HUMAN	known								
11	P13010 KU86_HUMAN	new								
12	Q13813 SPTA2_HUMAN	new								
13	Q961Z0 PAWR_HUMAN	new								
14	P27694 RFA1_HUMAN	new								
15	P61160 ARP2_HUMAN	new								
16	P10515 ODP2_HUMAN	new								
17	P42166 LAP2A_HUMAN	known								
18	O15145 ARPC3_HUMAN	new								
19	O75083 WDR1_HUMAN	new								
20	O15143 ARC1B_HUMAN	new								
21	Q01469 FABPE_HUMAN	new								
22	O75131 CPNE3_HUMAN	new								
23	P60903 S10AA_HUMAN	new								
24	P52294 IMA1_HUMAN	new								
25	Q9UNE7 STUB1_HUMAN	new								
26	P19105 MLRM_HUMAN	new								
27	P61158 ARP3_HUMAN	new								
28	Q92747 ARC1A_HUMAN	new								
29	Q01082 SPTB2_HUMAN	new								
30	Q8Y608 LRRF2_HUMAN	new								
31	P63092 GNAS2_HUMAN	known								
32	Q96CT7 CC124_HUMAN	new								
33	O15084 ANR28_HUMAN	new								
34	P53999 TCP4_HUMAN	new								
35	P50402 EMD_HUMAN	known								
36	O95816 BAG2_HUMAN	new								
37	O15144 ARPC2_HUMAN	new								
38	P08133 ANXA6_HUMAN	new								
39	Q9NZ01 GPSN2_HUMAN	new								
40	O60673 DPOLZ_HUMAN	new								
41	P35244 RFA3_HUMAN	new								
42	P52292 IMA2_HUMAN	new								
43	Q71D13 H32_HUMAN	new								
44	Q7Z7G8 VP13B_HUMAN	new								
45	P34931 HS70L_HUMAN	new								
46	P29084 T2EB_HUMAN	new								
47	Q13185 CBX3_HUMAN	known								
48	Q8WUQ7 CS029_HUMAN	new								
49	P14923 PLAK_HUMAN	new								
50	Q14839 CHD4_HUMAN	new								
51	P02452 CO1A1_HUMAN	new								
52	Q9HAZ2 PRD16_HUMAN	new								
53	Q92804 RBP56_HUMAN	new								
54	P42167 LAP2B_HUMAN	known								
55	Q8TD47 RS4Y2_HUMAN	new								
56	P59998 ARPC4_HUMAN	new								

57	Q5SRN2 CF01 O_HUMAN	new												
58	Q8IUQ4 SIAH1_HUMAN	new												
59	Q8NFG8 TCIP2_HUMAN	new												
60	P22492 H1 T_HUMAN	new												
61	Q9Y2T7 YBOX2_HUMAN	new												
62	P63208 SKP1_HUMAN	new												
63	P82094 TMF1_HUMAN	known												
64	Q96A08 H2B1 A_HUMAN	new												
65	P34947 GRK5_HUMAN	new												
66	Q52M93 Z585B_HUMAN	new												
67	P13942 COBA2_HUMAN	new												
68	P12235 ADT1_HUMAN	new												
69	Q9Y281 COF2_HUMAN	new												
70	Q8N257 H2B3B_HUMAN	new												
71	Q86UV5 UBP48_HUMAN	new												
72	O15131 IMA5_HUMAN	new												
73	Q15072 OZF_HUMAN	new												
74	Q9NY65 TBAB_HUMAN	new												
75	Q05639 EF1 A2_HUMAN	new												
76	O14974 MYPT1_HUMAN	new												
77	Q15233 NONO_HUMAN	new												
78	P54652 HSP72_HUMAN	new												

**Table4 : Microarray analysis**

	A	B	C	D	E	F	G	H	I
1	sample	W1,W2,W3,W4	W1,W2,W3,W4	P1,P2,P3,P4	P1,P2,P3,P4				
2	MeasurementID	W (RAW)	W (Processed)	P (RAW)	P (Processed)	Fold Intensity	regulation	Q-Value	GENE_SYMBOL
3	A_23_P10121	1949.083	1.1222653	559.56793	-1.0933652	4.644845369	down	6.31E-05	SFRP1
4	A_23_P101407	205.58698	-2.5984368	7399.8193	2.2750416	29.313196	up	5.05E-04	C3
5	A_23_P102364	5609.72	1.1263759	1701.5264	-1.0351338	4.47382795	down	2.83E-04	NGEF
6	A_23_P102611	367.88733	1.4622462	73.965385	-1.2184049	6.411452393	down	0.00131666	WISP2
7	A_23_P103601	2409.6934	1.416776	406.232	-1.5885901	8.029811414	down	3.69E-04	MAN1C1
8	A_23_P103877	257.6385	1.107465	85.44928	-0.92779744	4.09897315	down	0.00166683	LRRC38
9	A_23_P104073	1786.4855	0.8017895	781.1071	-0.81022644	3.056786846	down	7.88E-04	S100A3
10	A_23_P10542	1204.2821	1.6460173	152.04425	-1.7330652	10.40411562	down	4.46E-05	HTRA3
11	A_23_P10647	4074.7957	1.1773746	1124.4749	-1.083786	4.793769633	down	5.00E-04	CYTL1
12	A_23_P108501	269.755	1.1589456	74.01312	-1.1195382	4.851678135	down	5.00E-04	EPHA4
13	A_23_P108823	202.4681	-1.1403008	1179.9513	0.99527407	4.3941216	up	7.04E-04	OSBPL6
14	A_23_P109269	198.1326	0.94100964	73.46126	-0.89435637	3.568619303	down	1.93E-04	LAMA5
15	A_23_P111860	468.28683	0.8948326	187.24847	-0.85522187	3.363712591	down	6.31E-05	RADIL
16	A_23_P113613	402.2611	-1.4585474	3596.7466	1.2555287	6.561729	up	0.00183207	CDCP1
17	A_23_P114414	33.59012	-1.0810351	184.98561	0.93490434	4.044439	up	0.00155629	LONRF3

	A	B	C	D	E	F	G	H	I
18	A_23_P114423	308.29935	1.2688016	70.88101	-1.28306	5.863904064	down	7.46E-05	RGN
19	A_23_P114689	640.5663	0.96512604	215.77959	-1.0256959	3.974633887	down	5.64E-04	ASAP3
20	A_23_P114883	6993.5557	1.4918189	1386.4321	-1.1997037	6.45994832	down	0.00192356	FMOD
21	A_23_P115064	16315.2	1.2283618	4174.4355	-1.1457777	5.184265381	down	2.42E-04	CRABP2
22	A_23_P116264	1791.6968	1.1065145	664.80023	-0.7707913	3.673883337	down	0.00230223	NRGN
23	A_23_P120594	149.56468	0.9412221	50.26539	-1.06149	4.007526937	down	5.06E-04	ACSS1
24	A_23_P121637	102.87616	-0.9093934	518.5906	0.99659514	3.747656	up	2.22E-04	PRSS12
25	A_23_P121885	343.49896	1.2874718	101.373344	-0.91122234	4.590636635	down	0.00301133	ROPN1L
26	A_23_P12363	366.1189	0.9687958	132.49818	-0.8675462	3.571034482	down	0.0014113	ROR1
27	A_23_P125423	5993.8335	1.2622502	1627.2395	-0.9752302	4.715727683	down	0.00360391	C1R
28	A_23_P126089	34.46485	-1.1215664	215.2103	1.1159703	4.7159114	up	2.53E-04	SPRR2C
29	A_23_P12733	143.44452	1.6842468	18.941885	-1.6878085	10.35356171	down	1.67E-04	H2AFY2
30	A_23_P128174	57.537846	-1.0456678	310.44946	0.99252915	4.107319	up	3.84E-04	RAB3IP
31	A_23_P129005	514.66266	1.0715485	150.08162	-1.1483887	4.658731821	down	0.00258359	NYNRIN
32	A_23_P13094	16.267855	-1.7889042	268.78613	1.7835184	11.89615	up	1.02E-04	MMP10
33	A_23_P131263	67.007675	-0.91880906	306.54678	0.84545445	3.3970053	up	3.07E-04	MPP4
34	A_23_P131676	816.5483	1.7736065	112.27095	-1.4556234	9.377673223	down	0.00106487	CXCR7

35	A_23_P132159	1170.8888	1.0115061	410.06412	-0.92203903	3.819927108	down	0.00197986	USP18
36	A_23_P133293	46.11276	-1.8610101	555.39514	1.4065697	9.630294	up	0.00275598	MCTP1
37	<b>A_23_P133408</b>	<b>17.584705</b>	<b>-4.1047945</b>	<b>3677.7124</b>	<b>3.312037</b>	<b>170.87903</b>	<b>up</b>	<b>0.00461679</b>	<b>CSF2</b>
38	A_23_P134176	2937.7043	-1.2594943	20874.645	1.1443918	5.292268	up	9.22E-05	SOD2
39	A_23_P134835	2009.895	0.89285135	764.3793	-0.903301	3.472927419	down	1.86E-04	CSGALNACT1
40	A_23_P137016	1181.1946	-0.8823416	5328.7373	0.84933496	3.3211355	up	9.99E-05	SAT1
41	A_23_P137470	290.76956	0.9667978	104.851074	-0.9006635	3.648899397	down	9.57E-04	SIPA1L2
42	A_23_P138680	666.61066	0.9914439	251.62296	-0.8156514	3.499370288	down	0.00183207	IL15RA
43	A_23_P139143	102.49496	-0.85164106	431.24466	0.80381036	3.1502175	up	3.05E-04	STX3
44	A_23_P139912	45750.215	0.8914964	16980.357	-0.9561615	3.599154141	down	3.34E-04	IGFBP6
45	A_23_P140427	3164.2373	0.98663807	1126.3201	-0.9425149	3.808315304	down	1.83E-04	EVL
46	A_23_P140748	2595.8687	1.0301695	891.26874	-0.91495657	3.850714425	down	2.21E-04	NDRG4
47	A_23_P141429	343.79816	1.5105855	57.8985	-1.5034189	8.078035112	down	5.00E-04	ABI3
48	A_23_P142849	3362.5542	-0.8220825	14410.181	0.85045385	3.1877453	up	0.00162657	RND3
49	A_23_P142872	237.23782	1.773039	26.738317	-1.801672	11.91503153	down	9.10E-05	TCF7L1
50	A_23_P14302	3355.977	0.925858	1226.5398	-0.94324684	3.653058779	down	5.53E-05	C14orf139
51	A_23_P143190	1365.9084	0.95340943	517.43304	-0.8824322	3.5697959	down	3.21E-04	MYBL2

	A	B	C	D	E	F	G	H	I
52	A_23_P144476	267.0265	1.1516762	77.62152	-1.0060843	4.462216959	down	0.00150546	SPRY1
53	A_23_P145114	93.06875	-1.1300719	476.7817	0.850204	3.9456851	up	0.00159324	GCLC
54	A_23_P14515	750.27075	0.85849285	294.79724	-0.9162197	3.421698234	down	3.34E-04	ACOT4
55	A_23_P145935	268.30914	0.98292935	76.31889	-1.2605149	4.735261699	down	0.00417977	EPHB6
56	A_23_P146922	53.792698	-1.1027968	348.48215	1.163152	4.809706	up	2.57E-04	GAS6
57	A_23_P149121	156.38953	-1.1395619	1035.6754	1.1268532	4.811261	up	2.50E-04	DIRAS3
58	A_23_P149281	31.976458	-1.0713451	195.4946	1.1139034	4.548051	up	8.68E-05	EPHA2
59	A_23_P149545	27.562002	-1.0059456	132.69037	0.890259	3.7223265	up	0.00463113	HIST2H2BE
60	A_23_P150281	222.1926	1.1101408	58.622643	-1.2391254	5.095649676	down	3.63E-04	TP53I11
61	A_23_P150609	4064.3665	0.834522	1696.0723	-0.7991755	3.103072911	down	0.001919	IGF2
62	A_23_P15146	54.709526	-0.7760948	227.97588	0.8754078	3.1416068	up	0.001919	IL32
63	A_23_P151710	498.4145	1.4644558	93.01267	-1.4021052	7.293245426	down	2.85E-05	PTGER2
64	A_23_P151975	82.77395	-1.0377737	464.31754	1.0008729	4.1085997	up	0.00115091	RHCG
65	A_23_P152002	16.597757	-2.2712026	480.56885	2.1308076	21.14156	up	5.20E-05	BCL2A1
66	A_23_P152791	26.041405	-1.5992883	158.49922	0.7154459	4.97513	up	0.02354376	SLC16A6
67	A_23_P154605	297.74197	2.0327106	18.305895	-2.417928	21.86632399	down	4.15E-04	SULF2
68	A_23_P155755	606.8343	-1.1788418	3668.487	1.0345032	4.6374927	up	0.00298059	CXCL6

69	A_23_P156708	20502.057	1.1467674	6209.1953	-0.95624757	4.296062457	down	0.00211715	TNXB
70	A_23_P159952	1494.6116	-1.8255439	23136.268	1.689168	11.42967	up	9.97E-05	BEX1
71	A_23_P161218	14.901379	-1.6331618	174.93057	1.4998959	8.7729225	up	1.32E-04	ANKRD1
72	<b>A_23_P161698</b>	<b>26.833477</b>	<b>-5.4848156</b>	<b>48707.9</b>	<b>4.940816</b>	<b>1375.3961</b>	<b>up</b>	<b>8.17E-04</b>	<b>MMP3</b>
73	A_23_P161727	1432.7543	1.0202134	522.15094	-0.86956334	3.705778665	down	0.0019269	HSPB2
74	A_23_P16275	174.63235	1.4575638	28.901966	-1.569313	8.15043446	down	0.00144497	TSKS
75	A_23_P163402	65.2929	-0.9063997	305.54187	0.8797324	3.44889	up	3.29E-04	CYP1A1
76	A_23_P164057	7630.629	1.3850389	1771.5237	-1.0789301	5.51732509	down	0.00309797	MFAP4
77	A_23_P165783	161.3626	-1.0591307	890.3654	0.9589534	4.050455	up	0.00254723	MLPH
78	A_23_P166087	2927.3938	1.4972677	520.06335	-1.3983917	7.441840528	down	5.69E-05	RASSF2
79	A_23_P166297	189.31093	0.68165624	55.240326	-1.6362059	4.985927966	down	0.02431308	ABCG1
80	A_23_P166797	296.78625	1.4290576	56.20061	-1.3851358	7.033258875	down	1.71E-04	RTP4
81	A_23_P166848	58.52322	-0.9785664	283.04016	0.86820674	3.5969477	up	0.00105987	LTF
82	A_23_P167367	13.690687	-1.5387561	136.5354	1.3720733	7.520505	up	8.27E-04	PITX2
83	A_23_P167983	272.3631	-1.0362378	1461.072	0.9798002	4.044715	up	5.89E-04	HIST1H2AC
84	A_23_P168610	25.899992	-1.4376636	255.67638	1.3997506	7.147379	up	1.07E-04	TSPAN13
85	A_23_P17663	4026.7688	1.930764	425.75632	-1.7391291	12.72764021	down	4.35E-04	MX1

86	A_23_P1782	223.27863	-1.4313935	2314.5332	1.5160203	7.713651	up	6.02E-05	CD82
87	A_23_P18017	15.361082	-1.447836	140.34203	1.3253056	6.835949	up	0.0020113	CPA3
88	A_23_P1962	6617.2593	1.4771059	1285.6295	-1.3145657	6.924315843	down	0.00104794	RARRES3
89	A_23_P200710	343.53702	0.8162048	150.17845	-0.7978232	3.061052883	down	9.11E-05	PIK3C2B
90	A_23_P201459	10398.144	2.0124943	951.6782	-1.8311765	14.35688547	down	2.53E-04	IFI6
91	A_23_P202071	83.38672	-0.9656141	346.25964	0.70788217	3.189867	up	0.00479177	CUGBP2
92	A_23_P202448	15985.53	1.6802723	2209.2058	-1.5744479	9.544834522	down	4.37E-05	CXCL12
93	A_23_P204087	303.49814	1.3705155	51.35577	-1.6505351	8.117584181	down	6.45E-04	OAS2
94	A_23_P204751	358.44366	0.8978975	125.329475	-1.0543857	3.869864656	down	0.00471869	ACCN2
95	A_23_P205370	25.588142	-0.9127561	121.312874	0.9004718	3.514277	up	0.00280483	ASB2
96	A_23_P206733	80.717415	-1.2030247	487.36386	0.9484198	4.4427238	up	0.00330651	CES1
97	A_23_P207507	12.888317	-1.9279718	276.98224	2.0619094	15.888172	up	4.45E-05	ABCC3
98	A_23_P208210	63.289253	-0.9394139	280.44086	0.8174387	3.3796003	up	0.00123538	ZNF432
99	A_23_P210465	36.989204	-1.1622517	334.24673	1.5553256	6.5776725	up	0.00198136	PI3
100	A_23_P211522	1637.585	1.0851877	490.288	-1.0894849	4.514832897	down	2.55E-04	SYNGR1
101	A_23_P211631	17032.113	1.0238733	5439.6514	-1.0527298	4.218128716	down	3.02E-05	FBLN1
102	A_23_P21207	672.79767	0.7941239	294.2318	-0.82739496	3.07698812	down	6.72E-04	UBA7



103	A_23_P212089	46.075466	-1.3207706	348.9455	1.207886	5.7703404	up	0.00130544	NFKBIZ
104	A_23_P21363	3121.2295	0.8796761	1298.5933	-0.8217652	3.252256741	down	5.05E-04	AHNAK
105	A_23_P214026	2657.9087	1.050461	828.5382	-0.973475	4.066918376	down	0.00537191	FBN2
106	A_23_P214079	206.63562	-0.88434327	886.0408	0.7883327	3.1880538	up	0.00100397	SPINK1
107	A_23_P214144	43.318974	-2.8255162	3644.2913	3.115306	61.42788	up	6.31E-05	COL10A1
108	A_23_P214821	18.309952	-1.7948703	264.73584	1.6366756	10.789422	up	0.00126937	EDN1
109	A_23_P215634	8235.232	1.7004538	1354.2485	-1.1982565	7.457593699	down	0.00706848	IGFBP3
110	A_23_P215900	13244.992	0.88787556	5464.7847	-0.82847	3.286029838	down	2.22E-04	SCARA3
111	A_23_P216023	125.76207	-1.038451	555.29517	0.7414777	3.434092	up	0.00364284	ANGPT1
112	A_23_P216966	14858.253	0.7646539	6385.248	-0.86867356	3.102276792	down	0.0023194	PTGS1
113	A_23_P217319	688.287	2.5248854	24.744257	-2.701157	37.42790216	down	4.38E-04	FGF13
114	A_23_P22134	32.766148	-1.937252	614.9236	1.8715496	14.014046	up	3.02E-05	BNC1
115	A_23_P22350	247.39163	-0.84947765	1049.3751	0.8326297	3.2089634	up	3.77E-04	GRAMD3
116	A_23_P2283	35.381805	-0.9188857	161.74283	0.83082986	3.3629227	up	3.62E-04	TAC3
117	A_23_P24077	1606.1937	0.9695921	544.86206	-1.0122511	3.949974365	down	0.002695	C10orf54
118	A_23_P24716	4605.3325	-1.0129423	28690.05	1.1950593	4.6203485	up	3.34E-04	TMEM132A
119	A_23_P250358	171.38445	1.0386679	55.632072	-0.99373376	4.090852767	down	6.32E-05	HERC6
120	A_23_P251499	14912.597	0.9307976	5758.64	-0.84565973	3.425838979	down	4.65E-04	PCOLCE
121	A_23_P252062	1251.5892	1.1961248	313.7552	-1.227617	5.365608542	down	4.82E-05	PPARG
122	A_23_P252541	405.61957	1.1374819	115.35464	-1.1053995	4.733414565	down	4.82E-05	RAB7B
123	A_23_P253221	317.4141	-0.9405632	1642.2932	0.9994087	3.8369818	up	4.16E-04	ARHGEF4
124	A_23_P254741	18422.936	1.1136844	5998.1626	-0.88026714	3.983265188	down	8.88E-04	SOD3
125	A_23_P257003	291.18466	1.1758821	79.84735	-1.079702	4.775276446	down	0.00114592	PCSK5
126	A_23_P257649	388.1622	1.5715585	48.939556	-1.836299	10.61371245	down	7.71E-04	RBP1
127	A_23_P258769	1241.8488	1.5110216	248.10727	-1.2603073	6.827365556	down	0.00135347	HLA-DPB1
128	A_23_P259071	837.84894	-1.1417129	5939.935	1.1750429	4.982106	up	0.00179086	AREG
129	A_23_P259442	2683.9158	1.1530533	870.11664	-0.8257549	3.941673325	down	0.00563235	CPE
130	A_23_P26024	211.73592	-2.2154083	5572.722	2.068947	19.485853	up	9.27E-04	C15orf48
131	A_23_P26124	30.000992	-1.3120487	254.53812	1.3167602	6.1851516	up	5.33E-04	RORA
132	A_23_P27315	4487.2803	1.072628	1310.2317	-1.1140356	4.552514668	down	2.85E-05	EMILIN2
133	A_23_P29124	1054.9204	1.1387248	298.9345	-1.1167543	4.774928493	down	4.46E-05	5-Sep
134	A_23_P29939	49.42626	-2.1406221	1290.0631	2.1432142	19.478848	up	2.85E-05	SNCA
135	A_23_P301247	7815.1567	1.1910264	2749.6677	-0.7458403	3.828732378	down	0.0154497	HIST2H2AC
136	A_23_P302470	300.0849	1.356322	57.15892	-1.4720839	7.102888176	down	9.22E-05	SULT1B1
137	A_23_P30567	2579.1191	1.1980104	568.4359	-1.4441376	6.242604465	down	0.00189928	CRHBP
138	A_23_P30655	582.66077	-0.8443923	2396.9226	0.7617831	3.044437	up	0.00138947	NFKBIE
139	A_23_P315364	626.52167	-2.0396333	12556.196	1.9085863	15.43592	up	2.23E-04	CXCL2
140	A_23_P316612	160.61485	1.0334034	50.272438	-1.0871468	4.34859749	down	1.09E-04	GLIS1
141	A_23_P321846	34.61521	-0.77942336	150.4014	0.9258604	3.2609305	up	0.00183542	KCNS1
142	A_23_P32414	289.087	-1.071758	1557.0873	0.95900965	4.086222	up	4.38E-04	RP6-213H19.1
143	A_23_P3312	26285.438	0.8376858	11074.92	-0.8402877	3.199781903	down	3.02E-04	ISLR
144	A_23_P334870	47.650093	-0.94490147	215.32068	0.82716334	3.4154243	up	5.01E-04	TMEM217
145	A_23_P337729	533.3328	0.8990567	212.90585	-0.86992323	3.40812881	down	3.20E-04	TMEM180
146	A_23_P339098	276.04102	-1.1599997	1762.8695	1.0751288	4.708046	up	8.60E-04	SLC35F2
147	A_23_P342138	962.18665	0.84300256	371.52658	-0.97584176	3.527984591	down	5.77E-04	ADAMTSL1
148	A_23_P34375	752.76465	1.0100815	237.76868	-1.0661007	4.216898716	down	4.45E-05	TCEA3
149	A_23_P348257	374.03552	-0.9819057	1840.8488	0.91572714	3.7260134	up	1.96E-04	NUAK1
150	A_23_P355517	20.184444	-1.8077773	308.41547	1.6772091	11.196581	up	2.79E-04	SYNPO2L
151	A_23_P362694	321.74622	-2.3017256	7562.238	1.9096949	18.525242	up	8.78E-04	C4orf7
152	A_23_P363174	937.7749	0.9877479	384.28528	-0.75181293	3.339334897	down	0.01114404	HIST1H2AL
153	A_23_P366366	1163.7174	0.88199925	476.3185	-0.81414247	3.240332339	down	5.28E-05	SCRN1
154	A_23_P368484	253.70486	0.9793855	83.00975	-1.0511031	4.085431604	down	1.94E-04	C17orf76
155	A_23_P369994	311.9769	1.0644228	101.56105	-0.9399028	4.01201132	down	0.00261613	DCLK1
156	A_23_P373031	1252.4993	0.8578911	508.70145	-0.8941355	3.368313834	down	0.00296383	CACNA1C
157	A_23_P374844	724.84717	1.2530165	196.8602	-1.0792607	5.035996548	down	5.80E-04	GAL
158	A_23_P383819	31.412521	-0.93202364	130.01765	0.66661644	3.028577	up	0.00619332	TBX3
159	A_23_P38567	56.56805	-2.2602687	1633.1627	2.1454592	21.196114	up	3.19E-04	CYTSB
160	A_23_P38732	224.4155	-1.2594692	1713.6415	1.2357633	5.6381917	up	2.35E-05	CDH2
161	A_23_P388900	74.10068	-1.2865087	417.2423	0.8559623	4.4151754	up	0.003131	SLC22A15
162	A_23_P388993	306.32004	-0.9881495	1338.2452	0.751024	3.3384387	up	0.00198316	ZC3H12C
163	A_23_P389987	695.0881	0.87961364	307.40247	-0.73905396	3.07091297	down	0.00173243	TLX2
164	A_23_P393034	27.616285	-1.2131451	194.87183	1.1823374	5.2615304	up	3.20E-04	HAS3
165	A_23_P39465	4565.2456	1.823978	521.2682	-1.7180061	11.64778813	down	6.94E-04	BST2
166	A_23_P3956	114.99059	-0.85543966	524.94495	0.9065008	3.39154	up	1.05E-04	C10TNF1
167	A_23_P39955	242.5652	-2.625468	10822.214	2.4143906	32.896423	up	0.00111306	ACTG2
168	A_23_P401774	27.99377	-1.6630749	219.85503	0.9844191	6.265779	up	0.01085598	ELMOD1
169	A_23_P41114	149.08325	-0.967921	688.2046	0.87390924	3.584645	up	0.001919	CSTA
170	A_23_P41344	31.843643	-3.0864067	1200.7657	2.0377772	34.87652	up	0.00522403	EREG

171	A_23_P41476	729.65125	1.0533943	230.9625	-1.0241063	4.220753691	down	5.53E-05	SHISA3
172	A_23_P415021	1007.37573	1.2315133	235.87747	-1.2731386	5.675124437	down	6.31E-05	METTL7A
173	A_23_P415652	1437.2201	0.80746984	640.0584	-0.78413653	3.013847423	down	1.22E-04	GALNT12
174	A_23_P416894	29.036797	-1.0530393	201.62564	1.2711788	5.0079436	up	0.00353966	PION
175	A_23_P417918	158.69615	1.3601499	29.028614	-1.5272528	7.399370595	down	6.77E-04	PENK
176	A_23_P41804	1416.0282	1.2776825	312.07056	-1.3033373	5.983625092	down	7.46E-05	NKD2
177	A_23_P421011	2519.3628	1.17803	676.56323	-1.1392746	4.984002101	down	7.29E-04	KAZALD1
178	A_23_P422212	710.84546	-1.2407486	5599.841	1.2934849	5.7926903	up	1.96E-04	SLC35F3
179	A_23_P42257	5595.5474	-1.4777968	54771.906	1.3710947	7.204466	up	0.00273485	IER3
180	A_23_P425681	183.7669	-1.5519348	2105.9546	1.5173705	8.393691	up	1.12E-04	CCK
181	A_23_P42868	964.97205	0.94902515	323.8612	-1.0428874	3.977639303	down	0.00113252	IGFBP1
182	A_23_P43164	1704.1075	1.2424128	404.52313	-1.1730003	5.334722353	down	0.00304356	SULF1
183	A_23_P43276	1829.1023	1.0124652	585.5454	-1.0362742	4.137442873	down	4.64E-04	GPCR124
184	A_23_P433016	2465.725	1.1117802	731.48254	-1.0387778	4.439994583	down	1.83E-04	FBLN1
185	A_23_P44674	4237.535	1.4347336	721.603	-1.5322056	7.818756227	down	1.28E-04	CRIP1
186	A_23_P4551	566.491	1.2569113	142.14981	-1.1663895	5.363968315	down	4.93E-04	SETBP1
187	A_23_P45871	1010.6504	1.4550054	191.51978	-1.3083718	6.789837948	down	0.00136816	IFI44L
188	A_23_P46936	168.15613	-0.9942261	962.717	1.088109	4.234921	up	4.43E-04	EGR2
189	A_23_P47924	29.91783	-1.703411	310.4391	1.2613236	7.8068175	up	0.00235497	PTPRR
190	A_23_P4808	1244.7612	0.98986673	439.1443	-0.96008015	3.863603216	down	6.92E-04	PTGER1
191	A_23_P49009	521.4828	1.045299	166.86751	-1.0288414	4.210934821	down	1.90E-04	LPCAT4
192	A_23_P500381	325.38727	-1.0439136	1655.47	0.879539	3.7932978	up	3.36E-04	HTR7
193	A_23_P501007	29396.232	0.99758816	10574.471	-0.8597305	3.623335965	down	0.00269063	EFEMP1
194	A_23_P501634	129.15958	-0.90033305	578.2464	0.85985994	3.3874342	up	7.99E-04	BTN2A1
195	A_23_P502343	320.46384	1.221049	89.51007	-0.8864955	4.30957152	down	0.01490254	LPCAM33
196	A_23_P50946	252.80756	0.8829229	102.92137	-0.8177191	3.250455706	down	0.00199811	RAMP1
197	A_23_P51126	226.16748	0.8796518	95.03728	-0.8088454	3.223207922	down	8.53E-04	IL1RL1
198	A_23_P51187	1101.6	1.0137019	311.15073	-1.2386663	4.764643297	down	6.96E-04	PRKCZ
199	A_23_P51376	72.195595	-1.3574828	565.36035	1.167428	5.755379	up	5.89E-04	NKAIN1
200	A_23_P52986	168.64986	-0.83160615	703.2213	0.82172894	3.1455996	up	7.63E-04	VWCE
201	A_23_P53137	758.9225	2.386888	40.09871	-2.2738447	25.29416673	down	5.64E-04	HBG1
202	A_23_P53588	133.72713	-1.0585907	808.8563	1.0945776	4.4480352	up	1.97E-04	WNT5B
203	A_23_P53663	323.27902	-1.246107	1458.8416	0.52273345	3.4077995	up	0.02738287	PAWR
204	A_23_P55749	614.85834	1.2164848	146.09149	-1.2532077	5.539257214	down	6.72E-04	COL5A3
205	A_23_P56559	4611.294	2.8495817	146.33392	-2.57646	42.99335194	down	1.38E-04	DHRS9
206	A_23_P57199	36.015564	-1.0315521	173.812	0.8474064	3.6780944	up	0.00404693	GGTLC1
207	A_23_P57709	12339.703	1.1109436	3568.2483	-1.1049683	4.645751031	down	7.46E-05	PCOLCE2
208	A_23_P58251	1132.1229	1.386018	218.55078	-1.363029	6.722729299	down	1.55E-04	CPZ
209	A_23_P59807	208.32251	1.7472277	23.771408	-1.8271127	11.91197205	down	3.34E-04	WNT2
210	A_23_P62081	114.80429	-1.4485172	1172.2974	1.487256	7.6516633	up	1.18E-04	SCG5
211	A_23_P62188	735.9206	0.86866164	317.66843	-0.78353	3.143107442	down	2.11E-04	ZC4H2
212	A_23_P6263	1241.45	2.2871954	70.55574	-2.2712026	23.56213264	down	1.77E-04	MX2
213	A_23_P62752	116.541595	-2.0532436	2387.9683	1.8882236	15.363844	up	1.22E-04	NPPB
214	A_23_P62901	650.27826	0.88243103	245.66025	-0.9398811	3.536475062	down	1.38E-04	BTG2
215	A_23_P63660	142.13615	1.2916942	38.395306	-0.9987296	4.891998374	down	0.00115053	C10orf58
216	A_23_P64828	747.4204	2.054779	65.17817	-1.9032532	15.54126657	down	3.67E-04	OAS1
217	A_23_P64873	53453.06	1.4303145	12100.289	-1.0806205	5.699893971	down	0.00269063	DCN
218	A_23_P65442	2238.6575	0.96018195	878.8285	-0.81788754	3.429669315	down	7.66E-04	IRF9
219	A_23_P66798	440.75153	-1.6853895	6042.4756	1.6420312	10.038144	up	5.01E-04	KRT19
220	A_23_P67661	2475.298	1.2112532	619.7031	-1.2151289	5.375436909	down	5.83E-04	COX7A1
221	A_23_P67847	4078.7874	1.830925	473.74713	-1.7218807	11.7354859	down	5.53E-05	GALNT14
222	A_23_P68031	17.244715	-1.5776716	199.37465	1.5518287	8.751319	up	5.42E-05	STAT4
223	A_23_P69326	2651.9617	2.3036098	139.81415	-2.3641539	25.41773734	down	7.93E-06	CADPS
224	A_23_P69383	576.24316	1.1249332	186.93002	-0.88381386	4.024325761	down	0.00149673	PARP9
225	A_23_P69497	2992.2236	2.2170186	191.7943	-2.1609826	20.792643	down	3.02E-05	CLEC3B
226	A_23_P70818	656.4259	1.6281693	95.51476	-1.5975777	9.355061149	down	3.02E-05	SMO
227	A_23_P71037	1918.3821	-1.2241836	14787.92	1.2910621	5.71695	up	1.74E-04	IL6
228	A_23_P71144	19972.22	-1.0932806	118170.625	1.0953925	4.55886	up	0.00341189	CXCL1
229	A_23_P71530	4096.2026	1.3002121	930.69116	-1.2490153	5.853207754	down	1.90E-04	TNFRSF11B
230	A_23_P72668	453.49988	0.79405737	191.2649	-0.85818875	3.143226391	down	9.96E-04	SDPR
231	A_23_P72737	17885.543	2.2569797	1090.7417	-2.2070367	22.07002634	down	7.20E-05	IFITM1
232	A_23_P73420	360.10577	0.8420539	154.1402	-0.8297198	3.18606045	down	0.00156142	TRAPPC9
233	A_23_P73429	195.7334	-1.2045768	1464.9465	1.2733266	5.570873	up	1.12E-04	HCLS1
234	A_23_P74290	22.67836	-1.4394702	190.74121	1.2385834	6.3999176	up	0.00100397	GBP5
235	A_23_P75283	923.99774	1.3473656	196.41098	-1.3201392	6.353293837	down	1.96E-04	RPB4
236	A_23_P75786	939.48364	0.9025929	360.1665	-0.91350174	3.521267115	down	7.82E-04	SAL15A3
237	A_23_P76749	641.56995	0.9624753	212.77539	-1.0480354	4.029248151	down	0.00109083	GALNTL1
238	A_23_P76901	397.05682	1.1658211	111.27362	-1.1110679	4.846317223	down	8.30E-05	PLEKHG3

239	A_23_P78742	489.39148	1.2522988	126.978	-1.1276084	5.205032475	down	3.28E-04	FLT3LG
240	A_23_P78762	103.82074	-0.9193839	489.41803	0.8739157	3.466067	up	9.96E-04	HSD17B14
241	A_23_P79518	12095.953	-1.4243879	108502.97	1.2967374	6.5938697	up	0.00334601	IL1B
242	A_23_P82929	10444.37	1.6591554	1526.986	-1.5138578	9.01928612	down	1.77E-04	NOV
243	A_23_P83298	6927.586	0.83969903	3105.0715	-0.7731674	3.058589421	down	0.00154727	PRRX2
244	A_23_P87150	395.48056	-1.3022864	3080.3948	1.214138	5.721623	up	0.002899	LPXN
245	A_23_P87545	94091.85	1.0810084	29296.797	-1.0405095	4.351515226	down	5.44E-04	IFITM3
246	A_23_P89431	2589.6646	-0.91579175	11730.257	0.83368516	3.3623662	up	5.06E-04	CCL2
247	A_23_P8981	231.22327	1.6536999	31.736565	-1.6179452	9.657468334	down	1.55E-04	STAR
248	A_23_P90722	31.428509	-0.82064795	144.73962	0.94644916	3.4036841	up	3.07E-04	PTPRN
249	A_23_P90925	13.520733	-2.239828	391.13647	2.188521	21.531084	up	6.11E-05	IL1F8
250	A_23_P91334	681.8893	1.3123021	124.41982	-1.574176	7.394630034	down	0.00136511	HSPA12B
251	A_23_P91512	18.457024	-1.7834892	229.18503	1.3993554	9.080959	up	0.00230271	CLDN14
252	A_23_P93938	610.8655	1.1794562	182.2256	-1.0155683	4.578974512	down	5.89E-04	NACAD
253	A_23_P94103	955.64026	1.9100652	92.48979	-1.8627461	13.66876856	down	4.45E-05	SCARA5
254	A_23_P94338	1111.058	0.97192955	413.98596	-0.8015032	3.418664335	down	0.0059312	ENPP2
255	A_23_P94800	12166.02	0.99587727	4829.7363	-0.76052904	3.378554839	down	0.00540154	S100A4
256	A_23_P96369	29.253553	-0.9288833	168.26712	1.1713454	4.2877736	up	5.89E-04	CXorf57
257	A_23_P97606	738.80585	0.8349731	315.081	-0.83459926	3.181202706	down	8.78E-04	GSTM5
258	A_23_P98350	23.88463	-2.4960642	678.1415	2.0149667	22.801094	up	8.39E-04	BIRC3
259	A_23_P98645	723.0101	0.81987214	307.93036	-0.81644416	3.108710358	down	0.00344749	DCHS1
260	A_23_P9883	52.11023	-0.9120821	240.19595	0.83914995	3.3664594	up	0.00302071	NLRP3
261	A_24_P100517	1298.898	0.76415944	567.3978	-0.85137653	3.064254036	down	4.80E-04	C9orf140
262	A_24_P11315	1722.5615	0.94875073	702.5072	-0.73634243	3.215611718	down	0.00225553	OLFML3
263	A_24_P11506	224.5301	-1.3085651	1992.3182	1.3861101	6.47408	up	4.65E-04	KYNU
264	A_24_P120537	19.04616	-1.1371882	123.64075	1.1234938	4.79218	up	2.00E-04	SH3RF2
265	A_24_P12401	481.91446	-0.80308604	2013.5562	0.8281305	3.097741	up	5.05E-04	VEGFA
266	A_24_P142118	1454.0629	-0.95989656	5770.92	0.6585741	3.0704937	up	0.00550558	THBS1
267	A_24_P15502	33808.785	1.1532171	9858.357	-1.0652313	4.653926357	down	5.92E-04	
268	A_24_P160401	155.19751	-1.3928798	1349.697	1.249074	6.2417636	up	2.39E-04	CDCP1
269	A_24_P16124	27083.322	1.1989768	7409.306	-1.1082096	4.949169309	down	3.34E-04	IFITM4P
270	A_24_P16214	91.916046	-1.003369	410.596	0.7682276	3.414316	up	0.00106261	LOC100127980
271	A_24_P166443	865.5898	1.5694139	155.21056	-1.3490262	7.560282479	down	8.66E-04	HLA-DPB1
272	A_24_P179816	421.55188	0.81199956	173.31415	-0.90496063	3.287429854	down	0.00159092	SLC27A3
273	A_24_P183150	296.12323	-1.9117328	5461.422	1.8802583	13.851701	up	2.23E-04	CXCL3
274	A_24_P192727	6366.581	0.98813725	2208.664	-0.9595561	3.857572558	down	5.01E-04	
275	A_24_P212481	28.939457	-1.3184328	237.55684	1.2878864	6.089481	up	4.45E-05	MCTP1
276	A_24_P215765	717.15753	1.238466	168.60233	-1.2705084	5.692153321	down	4.45E-05	ATP10A
277	A_24_P228796	2231.6199	1.1007512	681.49384	-1.0409696	4.41288097	down	4.97E-04	GAGE7
278	A_24_P237270	24.548008	-0.93598974	120.24775	0.9512086	3.6991615	up	3.28E-04	ADORA2A
279	A_24_P250922	239.77066	-1.3475283	2164.382	1.3646593	6.5531464	up	3.18E-04	PTGS2
280	A_24_P252996	155.10478	-0.8448626	718.00165	0.93552804	3.4351916	up	4.32E-04	FOLR3
281	A_24_P257416	2086.7	-1.2477434	15067.982	1.1996636	5.454349	up	3.66E-04	CXCL2
282	A_24_P260639	12151.772	1.2771852	3888.9697	-0.8063855	4.238549643	down	0.01361669	HIST1H1D
283	A_24_P262127	61.428898	-1.4946	537.057	1.2303004	6.6111465	up	0.00100948	RRAD
284	A_24_P270460	3623.593	1.6927004	498.81067	-1.579493	9.661140333	down	3.96E-04	IFI27
285	A_24_P272761	170.0635	0.86506975	69.48293	-0.8711101	3.331518211	down	0.00168056	DENND1A
286	A_24_P277367	533.30756	-2.9206693	45724.383	3.0577464	63.049606	up	9.97E-05	CXCL5
287	A_24_P27977	465.66125	0.97150755	187.69763	-0.78174305	3.371172724	down	0.00265059	TRPM2
288	A_24_P287043	52918.953	1.161905	15160.01	-1.0803449	4.731343661	down	3.96E-04	IFITM2
289	A_24_P28722	1518.6523	1.4584496	242.85852	-1.5910667	8.279342362	down	3.20E-04	RSAD2
290	A_24_P291826	90.994156	-1.0663613	489.37372	0.92390513	3.9731038	up	0.00251273	SYTL3
291	A_24_P3005	88.32518	-0.95201814	355.88498	0.70021296	3.1431935	up	0.00617707	SCN9A
292	A_24_P300777	210.0231	-1.3903023	1777.5305	1.269352	6.3188157	up	2.21E-04	ADAM8
293	A_24_P304154	87.21439	-1.426415	823.9355	1.3925831	7.0567217	up	5.67E-05	AMPD3
294	A_24_P305784	33.72374	-1.7539726	476.2764	1.6159499	10.338268	up	7.09E-04	SPANXB2
295	A_24_P308029	1450.0278	0.96260905	465.52777	-1.1281884	4.259834574	down	0.00805029	HSPB6
296	A_24_P317762	6999.1963	1.1026449	2173.519	-1.0196424	4.353836653	down	5.05E-04	LY6E
297	A_24_P335305	896.386	1.1096716	259.9377	-1.1155807	4.67592606	down	4.82E-05	OAS3
298	A_24_P34155	170.51007	-0.9478049	873.10254	0.9686992	3.7750719	up	3.26E-04	RUNX1
299	A_24_P349196	227.29613	-1.0734823	1282.1764	1.0011361	4.21233	up	5.01E-04	CCDC30
300	A_24_P353905	1709.3411	0.8535321	715.89185	-0.84129214	3.237374531	down	4.43E-04	MXRA8
301	A_24_P366526	4415.9688	-1.1012056	25539.59	0.9823439	4.2384872	up	0.00347395	SYNGR2
302	A_24_P378019	6269.5527	1.0317626	2290.5298	-0.8537936	3.694953506	down	0.00123935	IRF7
303	A_24_P379820	886.7825	1.1778126	233.12073	-1.180127	5.126377509	down	2.21E-04	ITM2C
304	A_24_P380679	86.54875	-0.9623138	359.88025	0.74038696	3.2550974	up	0.00908254	C7orf53
305	A_24_P389916	4019.0486	1.2645862	845.5809	-1.4098475	6.38388116	down	0.00228428	LRRC32
306	A_24_P392110	19.709106	-2.1834173	438.8795	1.9416106	17.448463	up	5.26E-04	PSG8



307	A_24_P402080	598.9938	0.7894664	263.84766	-0.7964473	3.001978544	down	3.34E-04 MBP
308	A_24_P402690	5005.3413	1.2035878	1349.141	-1.1015317	4.942083965	down	6.28E-04 ITM2C
309	A_24_P40626	770.99243	1.2769852	191.43483	-1.0989531	5.190733503	down	0.00180618 GREM2
310	A_24_P408047	10913.412	1.3456733	2654.6943	-1.1409464	5.604632206	down	0.00160542 PLEKHA4
311	A_24_P412156	422.1029	1.5233425	69.55138	-1.44469	7.824685113	down	5.38E-04 CXCL12
312	A_24_P44462	1946.0173	-0.8498297	8646.468	0.86152554	3.274683	up	7.99E-04 TPM1
313	A_24_P48204	4895.8477	1.1800833	1419.2075	-1.044719	4.674468386	down	6.79E-04 SECTM1
314	A_24_P48723	6629.6973	1.5675235	932.7063	-1.6803663	9.499751178	down	0.00139437 PTGIS
315	A_24_P55496	757.016	1.2196035	198.131	-1.1551508	5.18647558	down	5.53E-05 OSR2
316	A_24_P557479	226.4415	0.968078	68.12204	-1.0979617	4.187355869	down	0.00540904 XAF1
317	A_24_P64167	4530.9263	0.84405494	1927.6434	-0.7785797	3.079368854	down	0.00102552 PTGS1
318	A_24_P678104	483.9349	1.0778034	148.7251	-1.0560083	4.388754851	down	3.02E-05 STMN3
319	A_24_P68908	45.05803	-1.1992996	231.90714	0.8248998	4.0676613	up	0.00515784 LOC344887
320	A_24_P694826	57.1825	-2.2245579	1313.1904	1.9423814	17.962786	up	0.00204969
321	A_24_P71244	31.82106	-1.2441118	242.36224	1.2488314	5.6292524	up	4.45E-05 PIK3CD
322	A_24_P80204	5660.609	2.4624875	243.99579	-2.5203483	31.62154325	down	7.20E-05 MALL
323	A_24_P827037	162.49008	-1.1370257	1034.4802	1.1319203	4.8197093	up	7.46E-05 LRRC15
324	A_24_P870620	345.74457	1.0539503	114.57913	-0.9355626	3.971028961	down	6.18E-04 PTN
325	A_24_P931443	194.93942	-1.6266097	2447.3748	1.5815248	9.241549	up	5.37E-04 GPR68
326	A_24_P941787	244.39998	-0.95539594	1033.2906	0.7644088	3.2939184	up	0.00626153 PRPF4B
327	A_24_P942068	111.291176	-1.1228461	697.486	1.1060293	4.687684	up	3.02E-05 TANC2
328	A_24_P945059	36.61296	-1.2582928	210.07037	0.9171548	4.5172586	up	0.00338923 MYCT1
329	A_24_P945113	259.4331	0.88937473	96.37831	-0.9584875	3.59966382	down	3.28E-04 ACVRL1
330	A_32_P108254	2224.6548	2.78185	59.38501	-2.850159	49.59108924	down	1.67E-04 FAM20A
331	A_32_P108655	80.46853	-1.0342747	462.06586	1.0180476	4.1477313	up	0.00126468 AK3L1
332	A_32_P112493	1499.8673	1.1854408	432.17233	-0.97534037	4.471568982	down	0.00183207 SGK493
333	A_32_P114284	149.12587	-0.94477785	633.59924	0.75671816	3.2523804	up	0.0063214 IKZF2
334	A_32_P119033	325.4973	2.2036679	22.095608	-2.057005	19.16859405	down	1.80E-04 PLCXD3
335	A_32_P125338	129.7524	1.4264559	22.82011	-1.5263147	7.74234408	down	2.16E-04 FAM43B
336	A_32_P142440	351.9913	1.9371437	34.75619	-1.7607801	12.97735076	down	5.92E-04 PCSK9
337	A_32_P157945	58.591484	-1.0215067	294.70184	0.9051378	3.8016994	up	4.80E-04 DSP
338	A_32_P164246	14.785448	-1.9215448	247.84795	1.7253287	12.52617	up	0.00100356 FOXQ1
339	A_32_P164593	758.25793	1.3752155	153.36705	-1.3252777	6.500241419	down	1.36E-04 ZMAT4
340	A_32_P192474	158.37967	1.0861924	59.066116	-0.78389263	3.655541271	down	0.00657842 PRRT1
341	A_32_P196142	1601.5603	-0.9567447	6781.0645	0.6891613	3.1294432	up	0.00806993 LOC100130938
342	A_32_P198731	749.24176	1.7063019	92.54323	-1.721049	10.7580973	down	3.69E-04 NEURL1B
343	A_32_P313405	429.37064	-0.8757596	2099.9048	1.0046077	3.6816878	up	4.62E-04 LAMA1
344	A_32_P32413	226.3146	1.2711802	55.557747	-1.1407217	5.321754614	down	0.0010408 SETBP1
345	A_32_P34444	206.44615	-1.7284204	3029.0156	1.7045002	10.799708	up	5.53E-05 FHOD3
346	A_32_P358887	47.340042	-1.6604047	627.8411	1.6271293	9.764418	up	3.02E-05 SLC4A4
347	A_32_P377880	32.538185	-1.4113393	303.32758	1.3772795	6.9096794	up	4.45E-05 GDNF
348	A_32_P37867	1282.6931	0.9643431	424.32043	-1.0529866	4.048337965	down	2.88E-04 KIAA1644
349	A_32_P54553	198.71811	0.9205463	72.86921	-0.94063354	3.633046335	down	0.00119256 USP41
350	A_32_P57810	153.77017	1.0434375	49.17733	-1.0341905	4.221126587	down	6.02E-05 RNF157
351	A_32_P68504	51.210434	-1.1583745	259.5749	0.82129765	3.9440346	up	0.00548381 ZDBF2
352	A_32_P70315	895.69794	1.1340034	244.0802	-1.1715748	4.943655673	down	4.32E-04 TIMP4
353	A_32_P83049	820.0527	1.1979315	193.0591	-1.3423169	5.816891357	down	3.07E-04 EFR3B
354	A_32_P85676	627.89935	1.3961856	116.98453	-1.4440455	7.161348256	down	2.85E-05 STK32B
355	<b>A_32_P87013</b>	<b>392.09186</b>	<b>-1.6952953</b>	<b>5655.9536</b>	<b>1.7310574</b>	<b>10.750655</b>	<b>up</b>	<b>8.23E-05 IL8</b>
356	A_33_P3214159	569.2901	-1.2797279	4297.2715	1.1812897	5.5060496	up	7.20E-05 CDH2
357	A_33_P3214466	199.76445	0.7313204	88.08407	-0.8766407	3.048207369	down	0.00261613 MESP1
358	A_33_P3214720	370.88647	-1.040953	1968.512	0.96465874	4.0155897	up	9.94E-04 ZC3H12A
359	A_33_P3215640	4850.002	1.308459	1056.1572	-1.2894547	6.054105053	down	8.96E-05 PI16
360	A_33_P3216133	151.70483	1.4099443	23.992678	-1.676687	8.495102022	down	0.00176213 ZMAT4
361	A_33_P3219596	460.78134	1.2822022	94.806465	-1.4220316	6.517117078	down	0.00135645 LOC254559
362	A_33_P3220470	663.86615	1.2712812	145.18814	-1.3401643	6.111156436	down	1.55E-04 SMAD6
363	A_33_P3220911	6994.054	1.7424119	796.1543	-1.8296988	11.89357557	down	4.45E-05 BST2
364	A_33_P3223056	210.4913	1.1275092	58.126724	-1.1094732	4.71409975	down	0.00144971 ADAMTS10
365	A_33_P3225512	314.7957	1.5209574	52.93675	-1.4622353	7.907341769	down	1.10E-04 OAS2
366	A_33_P3225522	535.32324	1.0051141	169.78355	-1.0878229	4.266156821	down	3.34E-04 OAS2
367	A_33_P3226212	86.391014	-0.9429573	399.1687	0.8452189	3.45378	up	1.69E-04 JAM2
368	A_33_P3227400	425.83997	1.0914024	113.2775	-1.1364385	4.684324101	down	0.0055206 COL4A4
369	A_33_P3227793	356.96918	0.90481544	125.10407	-0.99437296	3.730032901	down	0.00129663 CGREF1
370	A_33_P3229122	623.2011	0.8588176	268.23874	-0.88860476	3.357581338	down	0.03428638 HIST1H2BF
371	A_33_P3237150	207.14178	-1.2013388	1240.6694	0.95387554	4.454348	up	0.00214323 BMP2
372	A_33_P3238215	332.67487	-0.99824107	1416.7495	0.70773388	3.2624934	up	0.00380788 COBLL1
373	A_33_P3238290	14.34531	-1.931422	159.41792	1.3137882	9.482123	up	0.0060587 FAM65C
374	A_33_P3241269	131.23766	-2.6884027	6697.668	2.5737507	38.376564	up	1.22E-04 CES1

375	A_33_P3241511	270.31766	-1.0386833	1450.939	0.9378655	3.9355052	up	0.0065481	SERPIND1
376	A_33_P3242733	996.7806	1.2174909	287.82397	-0.9516165	4.4974508	down	0.00172385	SGK493
377	A_33_P3242863	552.0057	0.7953346	242.31812	-0.839877	3.106330951	down	3.99E-04	NT5M
378	A_33_P3243093	47.57673	-0.8348428	236.2221	1.0341091	3.6526713	up	5.89E-04	RGS5
379	A_33_P3243230	29.37938	-1.3749105	207.1229	1.0904353	5.522593	up	0.00191796	
380	A_33_P3243449	441.13776	1.5684624	73.350746	-1.4472518	8.087614094	down	4.15E-04	CD70
381	A_33_P3243887	448.34033	-1.565913	5517.2095	1.6008296	8.980168	up	6.14E-04	IL11
382	A_33_P3245178	179.74962	-0.91892076	718.5248	0.67814755	3.0252793	up	0.00435813	BEX2
383	A_33_P3246833	420.9798	-1.635591	5370.9023	1.5734358	9.247266	up	0.00120256	IL1RN
384	A_33_P3248354	255.07973	1.5064688	37.43329	-1.7168065	9.339046277	down	0.00232364	OLFM1
385	A_33_P3248439	412.9301	1.3939798	78.253204	-1.4507866	7.18389566	down	7.82E-04	FAM125B
386	A_33_P3248982	1808.5532	1.2329144	463.44046	-1.173343	5.300973646	down	1.33E-04	FAIM2
387	A_33_P3249534	611.5245	-1.4763739	6050.3984	1.4049437	7.3682275	up	2.16E-04	NEFM
388	A_33_P3249872	11419.395	1.1246264	3399.719	-1.0354857	4.469495869	down	8.81E-05	FBLN1
389	A_33_P3249976	32.857098	-1.2369808	128.99263	0.42593288	3.1665542	up	0.03777026	JAM2
390	A_33_P3251703	20611.22	1.3947625	3736.9277	-1.4910293	7.391113561	down	1.79E-04	CRIP1
391	A_33_P3252286	112685.62	0.8654027	48425.055	-0.7881341	3.146039632	down	2.53E-04	CRLF1
392	A_33_P3252695	3617.6504	1.2032232	1020.3369	-1.0229752	4.678994319	down	0.00199486	CYTL1
393	A_33_P3252781	4128.076	1.0312712	1250.9952	-1.1085277	4.407005852	down	6.52E-04	PLAC9
394	A_33_P3252785	2924.5193	1.1353874	833.29346	-1.098429	4.703766212	down	4.38E-04	
395	A_33_P3255304	5761.806	1.1718163	1527.6915	-1.1840298	5.118943778	down	0.00122948	GGT5
396	A_33_P3257678	21027.453	1.2382133	5824.5757	-1.1057124	5.076822478	down	0.00817213	HIST2H3A
397	A_33_P3258617	153.1983	-0.9217051	751.29816	0.9308617	3.6114216	up	8.03E-04	
398	A_33_P3262635	822.5578	0.9212756	321.8768	-0.8699992	3.461205853	down	7.88E-04	CECR1
399	A_33_P3265030	2068.6443	1.0255926	684.04486	-1.0112963	4.103596273	down	4.57E-04	5-Sep
400	A_33_P3266025	13.799548	-1.7033689	131.6409	1.222573	7.599697	up	0.00401423	LOC100131431
401	A_33_P3268892	81.0121	-1.0242467	503.7378	1.168916	4.573069	up	6.28E-04	
402	A_33_P3268910	700.39154	0.9727578	235.01433	-1.0182614	3.975177402	down	1.91E-04	
403	A_33_P3269636	5188.599	0.9694741	1761.3173	-1.0138996	3.954166466	down	8.68E-05	SBSN
404	A_33_P3270311	294.3153	-0.95649934	1395.4213	0.8796389	3.57053	up	3.28E-04	HECW2
405	A_33_P3270776	1097.3915	1.3524759	226.41498	-1.3326312	6.431286304	down	6.11E-05	HTRA3
406	A_33_P3271635	210.83083	1.8182515	26.8544	-1.6141601	10.79589963	down	1.53E-04	HLA-DPB1
407	A_33_P3271651	510.9501	1.5511298	89.79592	-1.4025149	7.747038133	down	1.79E-04	HLA-DPB1
408	A_33_P3275500	35.05438	-1.1163945	166.63864	0.78966534	3.7478414	up	0.00720564	LOC400743
409	A_33_P3276713	4297.838	1.4618647	816.64716	-1.3809679	7.174272771	down	7.20E-05	HGF
410	A_33_P3276718	2256.4583	0.78284836	991.91974	-0.8373735	3.074223152	down	1.39E-04	HGF
411	A_33_P3280521	28.216099	-1.458609	236.83755	1.231132	6.4519763	up	0.00110359	MFAP3L
412	A_33_P3280845	29953.527	0.9470253	11555.338	-0.8685832	3.520080652	down	5.64E-04	THY1
413	A_33_P3280993	100.96863	-0.88032544	418.29984	0.78192556	3.1650999	up	0.01099562	HCG18
414	A_33_P3283601	13103.127	1.0713615	4319.835	-0.95984626	4.087469058	down	3.34E-04	LOC389033
415	A_33_P3284404	2063.589	1.106215	602.6704	-1.105061	4.630846942	down	2.12E-04	SYNGR1
416	A_33_P3285545	1027.044	0.9645872	404.83185	-0.82012224	3.445490717	down	6.46E-04	CLDN4
417	A_33_P3287959	344.43677	0.79765356	149.46686	-0.8229319	3.074997844	down	2.35E-04	RASA4
418	A_33_P3290707	526.25916	-0.92190075	2242.844	0.77657485	3.2455783	up	0.00113252	MME
419	A_33_P3296497	85.442406	-0.9903923	343.13086	0.6669135	3.1542692	up	0.01327224	
420	A_33_P3298024	53.506447	-1.3879558	410.43787	1.1037619	5.6244726	up	0.00267308	ABCC3
421	A_33_P3298159	4615.4546	0.98157024	1837.0425	-0.71390533	3.238836395	down	0.00209978	PTGDS
422	A_33_P3298930	530.48065	-0.90903497	2245.438	0.7324934	3.1199617	up	0.01774734	LOC389300
423	A_33_P3301876	22.318764	-1.26624	129.01465	0.92221904	4.558183	up	0.00605089	HDAC4
424	A_33_P3302125	168.06772	-1.2139733	1004.0891	0.96618986	4.532048	up	0.02459556	LCE2A
425	A_33_P3302245	1511.8201	0.73337555	673.6803	-0.853848	3.004705399	down	0.00677361	TMEM59L
426	A_33_P3302632	755.1238	1.1333268	241.96672	-0.96722794	4.288742689	down	0.00581163	HIST1H2BE
427	A_33_P3304212	324.65042	1.2294074	79.31458	-1.2436887	5.552341059	down	5.28E-05	PLEKHG3
428	A_33_P3305105	177.93848	1.0869836	57.29771	-0.978552	4.185893172	down	4.32E-04	VWA5A
429	A_33_P3312658	16.689577	-1.8360565	221.49905	1.4886837	10.019511	up	0.0018633	
430	A_33_P3315779	136.731	0.8736584	58.012848	-0.75847626	3.099713122	down	0.002131	HERC6
431	A_33_P3316273	77.81615	-2.0083365	1464.8528	1.8031902	14.040543	up	0.00180934	CCL3
432	A_33_P3316539	716.89453	-1.3055232	4949.828	1.0983088	5.2920694	up	6.93E-04	SLC7A2
433	A_33_P3318581	2512.8196	-1.0518196	14183.905	1.0303297	4.2343755	up	1.72E-04	PLOD2
434	A_33_P3320538	54.335045	-1.0286744	246.52881	0.77937603	3.5016875	up	0.00709111	
435	A_33_P3325704	27.546455	-1.5926542	337.6577	1.5796461	9.014831	up	1.38E-04	SPRR2E
436	A_33_P3326588	979.5388	-1.0839813	4880.2	0.8323147	3.7745273	up	0.00360391	TNFRSF10D
437	A_33_P3329078	1349.3716	1.8115995	177.11375	-1.4728763	9.743741546	down	0.00237795	HBG1
438	A_33_P3329686	132.42297	0.924122	45.938103	-1.0437912	3.912018699	down	0.00360391	5-Sep
439	A_33_P3330264	5449.401	-0.9327204	25376.72	0.885607	3.526721	up	8.60E-04	CXCL1
440	A_33_P3332081	35.538223	-1.8033634	556.0937	1.7212648	11.508504	up	5.01E-04	KHDRBS3
441	A_33_P3341499	614.9284	-0.9351425	3292.2324	1.0443587	3.9435673	up	8.51E-04	WNT5A
442	A_33_P3342081	27.360016	-1.7744514	350.45502	1.4787502	9.534794	up	0.00159092	PRDM1

443	A_33_P3342917	27.222153	-0.97428167	139.67583	0.9691849	3.8462873	up	3.21E-04 SYNGR2
444	A_33_P3347291	885.57935	0.8842974	370.381	-0.805032	3.225067599	down	0.00100948 INMT
445	A_33_P3347869	58.376186	-2.8510718	2384.4526	2.2457356	34.22094	up	0.00209572 C3
446	A_33_P3348011	25.675642	-1.1754786	128.05997	0.6934755	3.6526766	up	0.01322066 LOC222699
447	A_33_P3350726	622.3606	1.0473847	173.88742	-1.2600044	4.949865289	down	7.24E-04 PPARG
448	A_33_P3351536	169.72058	0.8937571	58.218193	-1.0759734	3.916949239	down	0.00670301 PTK2B
449	A_33_P3351999	35.306046	-0.9766133	183.04651	0.97284937	3.8623066	up	7.46E-05
450	A_33_P3352970	403.82587	-0.95240855	2112.49	0.9884722	3.8393998	up	2.16E-04 IRAK2
451	A_33_P3353791	23.649208	-1.3371141	138.20837	0.93741393	4.838393	up	0.01392281 ITGA1
452	A_33_P3357530	3001.8584	0.968261	1088.7867	-0.9280224	3.722529639	down	5.53E-05 SLC12A7
453	A_33_P3360611	337.70468	0.8618028	143.24521	-0.81193185	3.190394106	down	1.68E-04 MPP2
454	A_33_P3362008	50.2169	-2.076064	999.61694	1.8281782	14.97249	up	3.48E-04 NPPB
455	A_33_P3364864	332.55402	-1.0714716	1845.1512	0.99492073	4.1883802	up	6.48E-04 NAMPT
456	A_33_P3364869	200.9327	-1.5581995	1504.3467	1.0446255	6.0747504	up	0.00965895 NAMPT
457	A_33_P3369844	91.823746	-1.0074241	486.77277	0.9501262	3.8840191	up	8.03E-04 CD24
458	A_33_P3370094	412.4511	-0.98945284	1860.8416	0.8110366	3.4833837	up	0.00230271 MME
459	A_33_P3371718	823.50037	-0.88610077	3837.5142	0.8813791	3.4045873	up	2.16E-04 SAT1
460	A_33_P3375934	638.9062	-1.136586	3570.2212	0.94721055	4.239213	up	0.00131666 NAMPT
461	A_33_P3376140	11.002714	-1.6585754	110.218	1.2864639	7.7009654	up	0.01788862 KCNJ15
462	A_33_P3379091	218.78568	0.80558205	85.408424	-0.98491454	3.459339785	down	0.00267226 SYNGR1
463	A_33_P3379886	46.88617	-1.596421	354.0429	1.0222149	6.1416907	up	0.00471342 FGF2
464	A_33_P3381338	5872.6733	1.1042354	1709.105	-1.0478117	4.44458035	down	5.01E-04 TNXB
465	A_33_P3382856	5243.6953	1.6728835	892.1293	-1.2329383	7.494445679	down	0.00354705 DCN
466	A_33_P3384287	5493.972	2.0385697	448.68274	-1.9958379	16.38617898	down	2.35E-05 PALM
467	A_33_P3393135	186.15112	0.8962575	80.62615	-0.7629783	3.158491858	down	0.00918312
468	A_33_P3393821	43659.89	1.2569795	11857.388	-0.9830487	4.72406277	down	0.00301133 C1R
469	A_33_P3394727	31.028233	-1.819315	444.23798	1.6282737	10.910071	up	4.62E-04 KHDRBS3
470	A_33_P3395605	3371.995	1.1464863	1048.6815	-0.98203254	4.37268327	down	6.52E-04 TMEM119
471	A_33_P3396527	152.6982	-0.90719473	627.3004	0.7295804	3.1096995	up	0.00380643 POLR3G
472	A_33_P3397763	322.81003	1.2687835	87.20468	-1.0514137	4.994004697	down	9.96E-04 TNFSF9
473	A_33_P3401647	705.0443	0.79246974	312.26202	-0.8161149	3.049525204	down	0.00530638 PPP1R14A
474	A_33_P3401826	200.70169	1.44673	33.563457	-1.5789143	8.143475	down	9.97E-05 CMPK2
475	A_33_P3404480	70.636925	-0.9639337	345.95013	0.8899648	3.6147566	up	3.80E-04 MPP4
476	A_33_P3406493	751.32947	1.1714735	198.17238	-1.1870008	5.12827745	down	5.28E-05 GABBR2
477	A_33_P3407529	643.5459	1.7279105	67.23547	-1.9800355	13.06781536	down	8.26E-04 PRRT4
478	A_33_P3408953	51.826603	-0.9262401	218.02252	0.7587609	3.2154062	up	0.0029287 GGTLC2
479	A_33_P3409210	222.51572	1.1668302	67.98511	-0.9987732	4.486540356	down	2.77E-04
480	A_33_P3409477	44.2302	-0.8451568	199.99277	0.9020066	3.3569787	up	1.96E-04 UBASH3B
481	A_33_P3413987	178.93347	0.94564426	63.62398	-0.98902094	3.822894036	down	2.21E-04 SERPING1
482	A_33_P3415340	28.778248	-1.0569726	141.20045	0.85920703	3.774223	up	0.00176193
483	A_33_P3416473	149.87825	-1.0585933	807.3224	0.94567394	4.011849	up	3.37E-04 LOC646999
484	A_33_P3419190	286.4323	-1.1598163	2059.5295	1.1689951	5.023913	up	0.0021501 AREG
485	A_33_P3419696	165.64836	-1.3860646	1139.5737	1.0485809	5.4063153	up	0.00347395 FGF2
486	A_33_P3421243	55.156227	-0.9722979	267.4368	0.89407754	3.646154	up	0.00113216 AFP
487	A_33_P3423551	3446.686	-1.408222	31988.645	1.3598528	6.8119826	up	0.00187072 IER3
488	A_33_P3423941	7677.913	2.3382368	408.90033	-2.3175225	25.20712061	down	5.32E-05 IFITM1
489	A_33_P3441021	387.67456	-1.2326658	2977.273	1.2706738	5.669964	up	8.17E-05 TMEM233
490	A_33_P3695899	18.985786	-1.303551	126.652756	1.0751868	5.2008157	up	0.00198593 FLJ31104
491	A_33_P3712341	1125.8806	1.4256968	211.75423	-1.3886632	7.034072696	down	3.88E-05 CXCL12
492	A_33_P3718269	112.25133	-1.8618915	1929.4307	1.8415062	13.026682	up	2.21E-04 LOC285628
493	A_33_P3775848	622.7465	0.725693	243.07455	-1.0922316	3.525736288	down	0.00521031 CLIC2
494	A_33_P3813128	62.090183	-1.0839242	403.36728	1.1818702	4.809191	up	1.55E-04 SEMA3F
495	A_33_P3825869	682.66125	1.5376301	110.27188	-1.5242189	8.350422055	down	3.02E-05 CACNA1C
496	A_33_P3835524	56.407463	-1.0043668	327.781	1.0911775	4.273874	up	0.00102514 POU2F2
497	A_33_P3846177	1333.5537	1.3600705	266.11856	-1.404554	6.795711335	down	1.19E-04 B4GALNT1
498	A_33_P3846653	19.00562	-1.6230434	269.7326	1.7695615	10.502092	up	6.10E-04
499	A_33_P3871347	2264.1577	1.0686228	705.47473	-1.0133078	4.233734131	down	1.21E-04 SNED1

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