Universidad Europea

GRADUATION PROJECT

Degree in Dentistry

IN SILICO ANALYSIS TO IDENTIFY DIFFERENTIALLY EXPRESSED GENES IN PATIENTS WITH PERIODONTITIS

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ABSTRACT

Introduction: Periodontitis is a chronic multifactorial inflammatory disease characterized by the progressive destruction of tooth-supporting tissues, driven by complex interactions between bacterial biofilms and the host immune response. Recent advances in transcriptomic technologies have enabled the identification of gene expression changes associated with disease progression. **Objective:** The aim of this study was to identify and analyze differentially expressed genes (DEGs) in gingival tissues from patients with periodontitis compared to healthy controls. **Materials and methods:** An in silico RNA sequencing analysis was performed using publicly available datasets processed on the Galaxy platform. Data quality was assessed with FastQC and MultiQC, transcript quantification was carried out using Salmon, and differential expression analysis was performed with DESeq2. Gene annotation and functional enrichment analyses were conducted using Gene Ontology and KEGG pathway databases. **Results:** The analysis revealed a clear separation between healthy and periodontitis samples based on gene expression profiles. A large number of genes were significantly differentially expressed, with a predominance of upregulated genes in periodontitis. Notably, genes such as IL1B, CXCL3, SELE, and SLC1D1 showed increased expression, while KRT14, NPTX1, and CD1A were downregulated. Heatmap and MA plot analyses confirmed consistent expression patterns across samples. Functional enrichment highlighted pathways related to immune response, cytokine signaling, and leukocyte migration. **Conclusions:** Periodontitis is associated with a distinct transcriptional profile characterized by coordinated upregulation of immune-related genes and pathways, supporting its classification as an immune-driven disease and highlighting potential molecular targets for diagnosis and therapy.

KEY WORDS : Dentistry, periodontitis, RNA-seq, differential gene expression, transcriptomics .

RESUMEN

Introducción: La periodontitis es una enfermedad inflamatoria crónica multifactorial caracterizada por la destrucción progresiva de los tejidos de soporte dental, impulsada por complejas interacciones entre los biofilms bacterianos y la respuesta inmunitaria del huésped. Los avances recientes en tecnologías transcriptómicas han permitido identificar cambios en la expresión génica asociados con la progresión de la enfermedad. **Objetivo:** El objetivo de este estudio fue identificar y analizar los genes diferencialmente expresados (DEGs) en tejidos gingivales de pacientes con periodontitis en comparación con controles sanos. **Materiales y métodos:** Se realizó un análisis in silico de secuenciación de ARN utilizando conjuntos de datos públicos procesados en la plataforma Galaxy. La calidad de los datos se evaluó mediante FastQC y MultiQC, la cuantificación de transcritos se llevó a cabo con Salmon y el análisis de expresión diferencial se realizó con DESeq2. La anotación génica y los análisis de enriquecimiento funcional se realizaron utilizando las bases de datos Gene Ontology y KEGG. **Resultados:** El análisis reveló una clara separación entre las muestras sanas y las de periodontitis basada en los perfiles de expresión génica. Un gran número de genes se expresó de manera diferencial de forma significativa, con predominio de genes sobreexpresados en la periodontitis. En particular, genes como IL1B, CXCL3, SELE y SLC1D1 mostraron una mayor expresión, mientras que KRT14, NPTX1 y CD1A estuvieron subexpresados. Los análisis de heatmap y MA plot confirmaron patrones de expresión consistentes entre las muestras. El análisis de enriquecimiento funcional destacó vías relacionadas con la respuesta inmunitaria, la señalización de citocinas y la migración de leucocitos. **Conclusiones:** La periodontitis se asocia con un perfil transcripcional distintivo caracterizado por la sobreexpresión coordinada de genes y vías relacionadas con el sistema inmunitario, lo que respalda su clasificación como una enfermedad impulsada por mecanismos inmunitarios y resalta posibles dianas moleculares para el diagnóstico y el tratamiento.

PALABRAS CLAVE : Odontología, periodontitis, RNA-seq, expresión génica diferencial, transcriptómica.

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1. INTRODUCTION

Periodontitis is a chronic multifactorial inflammatory disease characterized by the progressive destruction of the tooth-supporting structures, including the gingiva, periodontal ligament, and alveolar bone. It results from a complex interaction between pathogenic bacterial biofilms and the host immune response, ultimately leading to tooth loss if left untreated (1,2). Clinically, it is manifested by periodontal pocket formation, gingival bleeding, and the loss of clinical attachment (CAL) with corresponding alveolar bone resorption visible on radiographs (3). The principal bacterial species implicated in periodontitis is *Porphyromonas gingivalis*, a Gram-negative anaerobic rod commonly found in subgingival plaque within periodontal pockets. Beyond its local effects, periodontitis has been linked to systemic diseases such as diabetes mellitus, cardiovascular disease, and rheumatoid arthritis, underscoring its relevance as a major public health concern (2,4). The primary intention of periodontal treatment is to stop the inflammatory process by eliminating local irritant factors (5). Basic treatments include oral hygiene instructions, scaling and root planing, and the use of chemical agents to control bacterial plaque (5).

Recognized as an eco-genetic disease, periodontitis is influenced not only by microbial factors but also by genetic polymorphisms, variations in the host immune and inflammatory responses, and a range of local, environmental, and systemic conditions (6). In this context, focusing on genetic polymorphism may play a key role in improving both the diagnosis of periodontitis and the development of more targeted and effective treatment strategies (1).

Recent advances in high-throughput transcriptomic technologies, including RNA sequencing (RNA-seq), have provided valuable insights into the molecular mechanisms underlying periodontitis. These approaches enable the identification of differentially expressed genes (DEGs) and signaling pathways involved in inflammation, immune regulation, tissue destruction, and repair (1,2,7).

Early transcriptomic studies demonstrated that genes related to immune response, cytokine signaling, and extracellular matrix remodeling are strongly up-regulated in diseased gingival tissues compared to healthy controls (1,2,7). For instance, Davanian et al. identified distinct gene expression profiles in paired gingival biopsies from periodontitis-affected and healthy tissues, revealing the activation of pathways involved in host defense and tissue degradation (1). This study found 453 significantly DEGs, such as IRF4 and CCL18, which are proteins expressed in inflammatory processes, not only in periodontitis but also in several chronic inflammatory diseases (1). Similarly, Kebschull et al. classified different periodontitis phenotypes based on

gingival transcriptomes, suggesting that the expression of these different phenotypes according to distinct gene expression patterns can be used for a new classification of periodontitis (2). Currently, periodontitis is classified according to biological effects, including evidence of progression direct or indirect, risks factors and progression (3).

More recent research has expanded these findings by integrating large-scale transcriptomic datasets and machine learning analyses. Moreno et al. conducted a meta-analysis of RNA-seq data and proposed potential diagnostic biomarkers and drug targets for periodontitis (4). This study revealed 22 significant genes considered excellent diagnosis biomarkers, such as MZB1, MERTK, SCAMP5, C7, CR2, SMPDL3B, SLC17A9, BMP6, ST6GAL1, C1orf68, and LAX1 (4). Furthermore, single-cell RNA sequencing has uncovered novel oxidative stress–associated biomarkers, offering new perspectives on the molecular heterogeneity of periodontal lesions (8). This research highlights the expression of COL4A2, CXCL and CYR61 which can serve as useful biomarkers for diagnosis as they are significantly up-regulated in periodontitis group compared to healthy one (8).

Collectively, these studies highlight that periodontitis is not a uniform disease entity but a spectrum of molecularly distinct conditions driven by dysregulated immune and inflammatory pathways. Understanding differential gene expression patterns between healthy and diseased periodontal tissues provides a foundation for identifying biomarkers and potential therapeutic targets (4,8,9). Despite the abundance of evidence, there is a lack of comprehensive meta-studies that put everything in context. The present work aims to fill this gap by synthesizing current knowledge into a unified framework.

2. OBJECTIVES

General objective: to characterize the transcriptional profile associated with periodontitis by comparing gene expression patterns between healthy and diseased gingival tissues.

Specific objectives:

1. To identify the genes that are differentially expressed between healthy and periodontitis gingival tissues.
2. To determine whether genes related to immune response, cytokine signaling, and leukocyte migration are upregulated in periodontitis.
3. To analyze whether genes associated with tissue homeostasis and structural integrity are downregulated in periodontitis.

Hypotheses:

- Null hypothesis (H0): There are no differences in gene expression patterns between healthy and periodontitis gingival tissues.
- Alternative hypothesis (H1): Periodontitis gingival tissues present a distinct transcriptional profile compared with healthy tissues.

3. MATERIALS AND METHODS

Department code : OD.071/2526

CI code : 2026-194

The sequencing data used in this study were obtained from the NCBI Sequence Read Archive (SRA), specifically from three BioProjects : ID : 929043 (10), ID : 723754 (11), ID : 319790 (12). These datasets include gingival tissue samples from both healthy individuals and patients with periodontitis, identified by SRR accession numbers corresponding to individual sequencing runs. In total, 46 samples were included in the analysis. (Table S1)

All analyses were performed on the public Galaxy server (https://galaxy-main.usegalaxy.org/). Raw sequencing data were retrieved from the NCBI Sequence Read Archive using “Faster Download and Extract Reads in FASTQ” (Galaxy Version 3.1.1+galaxy1). Read quality was assessed using FastQC (Galaxy Version 0.74+galaxy1) (See Supplementary Figure S1 and S2), and summary quality metrics across samples were aggregated using MultiQC into a single report (Galaxy Version 1.33+galaxy0). Transcript sequences were generated from the GENCODE v49 basic gene annotation (reference chromosomes only) using gffread (Galaxy Version 2.2.1.4+galaxy0). Transcript abundance quantification was performed using Salmon quant (Galaxy Version 1.10.1+galaxy4). A decoy-aware index was constructed within the same tool using the GENCODE v49 transcriptome and the GRCh38 primary genome assembly as decoy sequences. Quantification was performed in quasi-mapping mode with selective alignment enabled (--validateMappings), automatic library type detection, and sequence-specific and GC bias correction activated. Transcript-level abundance estimates were summarized to gene-level counts within Galaxy and analyzed for differential expression using DESeq2 (Galaxy Version 2.11.40.8+galaxy2), applying the poscounts size factor estimator and a parametric dispersion fit with default independent filtering and Cook’s distance handling. Differential expression results were annotated using Annotate DESeq2/DEXSeq (Galaxy Version 1.1.0+galaxy1) with the

corresponding GENCODE v49 basic GTF file to retrieve gene symbols and biotype information. All plots were generated with R studio 2026.01.0 Build 392.

4. RESULTS

To evaluate global transcriptional differences between healthy and periodontitis samples, PCA was performed on gene expression data (Figure 1). Each point represents an individual sample, colored according to clinical condition (healthy in red, periodontitis in blue) and shaped according to the study of origin (Hyunjin, Jung, Kim). The first principal component (PC1), explaining 27.4% of the variance, primarily separates samples based on disease status, while the second principal component (PC2), accounting for 20.5% of the variance, reflects additional variability within the dataset. A clear separation between healthy and periodontitis samples is

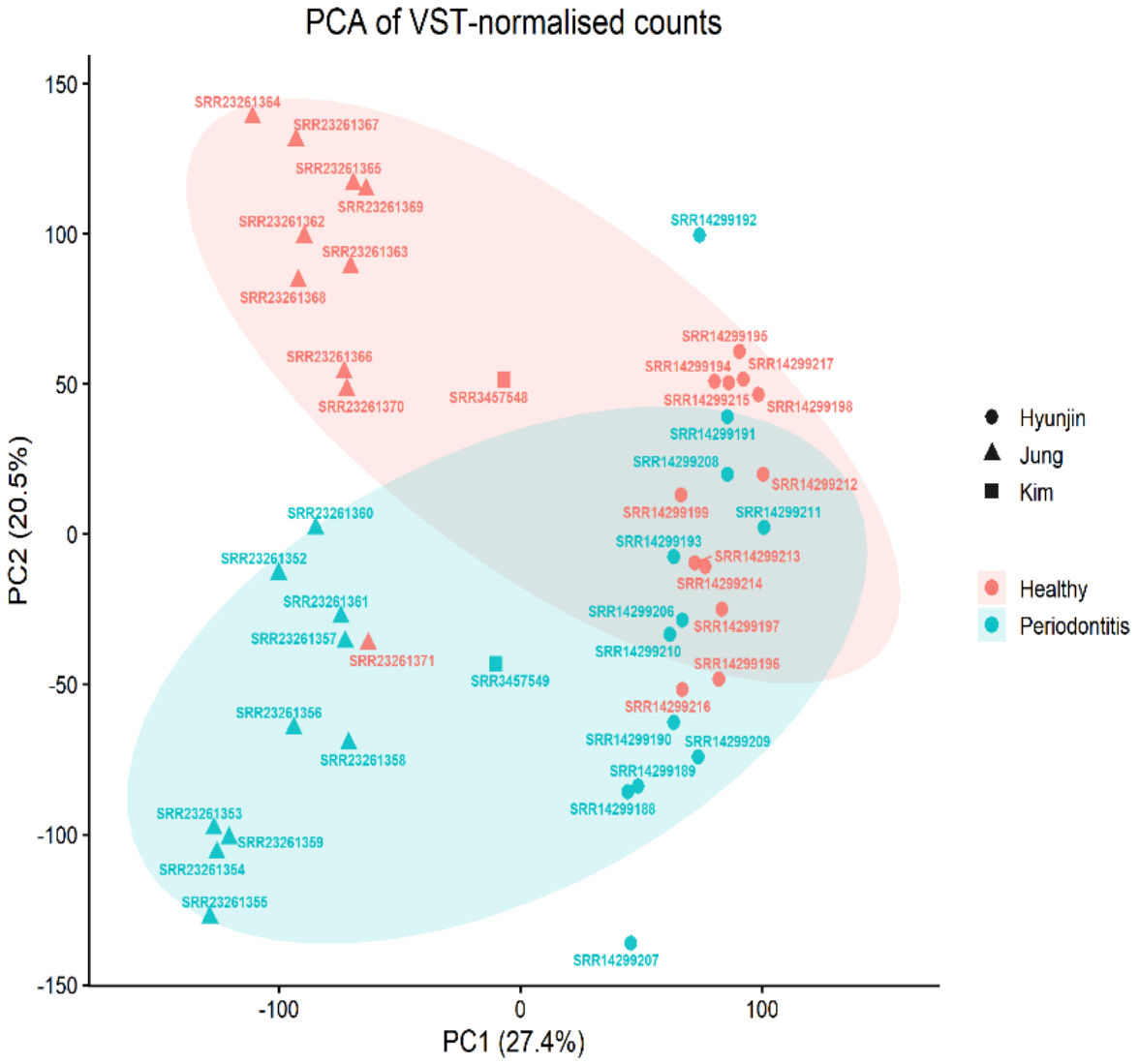


Figure 1: PCA (Principal Component Analysis) of gene expression in healthy and periodontitis gingival tissues

observed, indicating distinct overall transcriptional profiles associated with disease status. Samples also show partial clustering according to their study of origin, highlighting the presence of dataset-specific variation. Ellipses represent the overall distribution of each group and illustrate the dispersion and partial overlap between conditions.

Differential gene expression analysis was then conducted using DESeq2, considering genes with an adjusted p-value (padj) < 0.01 as statistically significant. The results for protein-coding genes are summarized in the volcano plot (Figure 2), which displays the relationship between $\log_2$ fold change and statistical significance, where each point represents an individual gene. Only protein-coding genes were included in this representation to focus on genes with well-characterized biological functions and to improve interpretability, as non-coding transcripts are often less functionally annotatsed and may introduce additional complexity. Numerous genes were significantly differentially expressed between conditions, with upregulated genes shown in orange and downregulated genes in blue. The top 25 upregulated and top 25 downregulated genes are presented in Supplementary (Table S2.1 and S2.2). A predominance of upregulated genes is observed in periodontitis samples, suggesting an overall activation of transcriptional programs associated with the disease. Among the most strongly upregulated genes in periodontitis samples were SLC6A5, INHBE, FCRLA, MEI1, IRF4, KCNN3, OSM, TENT5C, RIMS2,

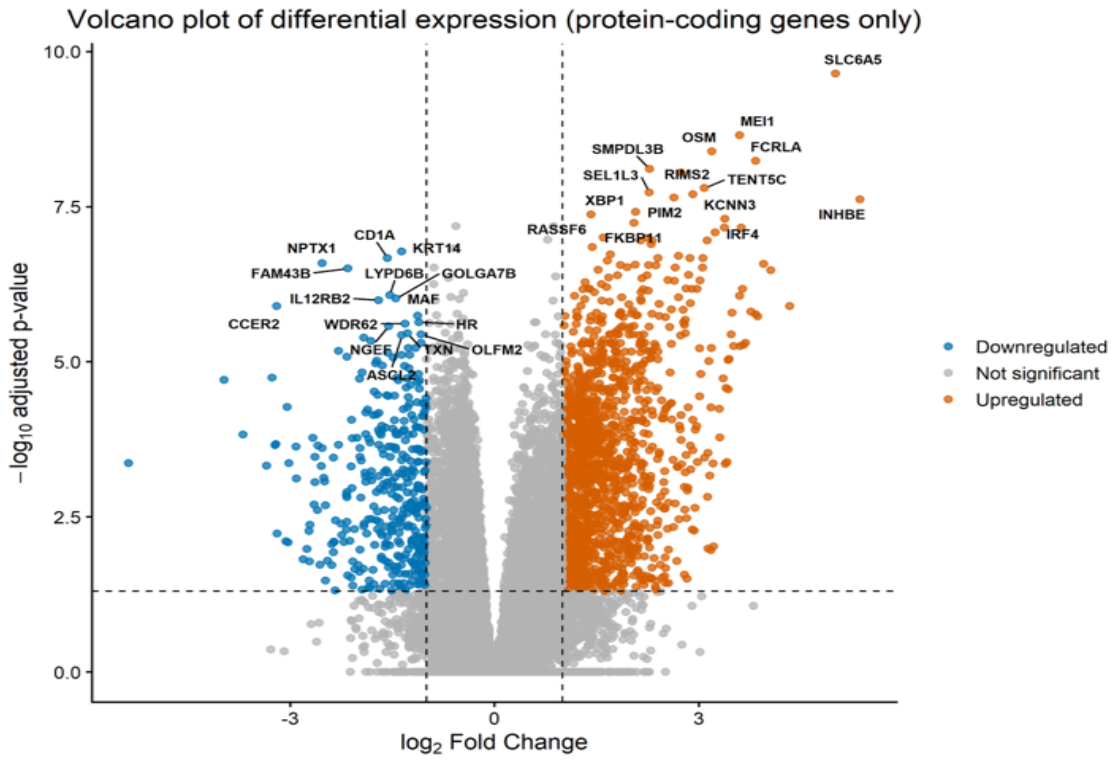


Figure 2 : Volcano plot of diffaerential expression (Protein-coding genes only)

SMPDL3B, SEL1L3, PIM2, FKBP11, and XBP1, many of which are related to immune and inflammatory responses. In contrast, genes such as CCER2, NPTX1, FAM43B, WDR62, IL12RB2, CD1A, LYPD6B, NGEE, KRT14, ASCL2, GOLGA7B, TXN, HR, and OLFM2 were among the most downregulated, indicating potential alterations in epithelial integrity and tissue homeostasis. Overall, these results highlight substantial and coordinated transcriptional reprogramming associated with periodontitis, reflecting both the activation of immune-related pathways and the downregulation of genes involved in tissue homeostasis.

To further explore gene expression patterns across samples, a heatmap of the top 50 differentially expressed protein-coding genes was generated (Figure 3). The heatmap shows a clear separation of samples based on their expression profiles. Samples cluster into two main groups, corresponding to oral health status, indicating consistent differences in gene expression patterns between these conditions. Within the heatmap, color gradients range from blue (lower expression) to red (higher expression), highlighting the most strongly differentially expressed genes across samples.

A distinct cluster of genes displays increased expression (red) predominantly in the periodontitis group, while showing lower expression (blue) in healthy samples. This pattern is particularly evident for genes such as IL1B, CXCL3, SELE, SLC1D1, NEDD9, CREB3L2, and DBMT1**,** which appear consistently upregulated in periodontitis samples. Conversely, another set of genes shows relatively higher expression in healthy samples and reduced expression in periodontitis, including CD1A, NPTX1, KRT14, FAM43B, and RTN4R**.**

The hierarchical clustering of both genes and samples reveals groups of co-expressed genes, forming distinct expression blocks across the heatmap. Although a minor clustering according to study of origin can be observed, the separation between healthy and periodontitis samples is more pronounced, indicating that disease status is the primary driver of the observed expression patterns, rather than technical or dataset-related variability. Some genes, such as CSF2RB, FCRLA, and PARM1, exhibit intermediate patterns but still contribute to the separation between sample groups. Overall, the strongest differential signals are visible as vertical bands of red or blue across subsets of samples, indicating coordinated up- or down-regulation.

These results demonstrate that the selected top 50 genes effectively discriminate between sample groups, with clear clustering and consistent expression differences across conditions.

In support of these observations, differentially expressed genes are distributed across a wide range of expression levels rather than being restricted to low-expression regions. This indicates that the observed differences are not driven by low-count artifacts, but also involve genes with

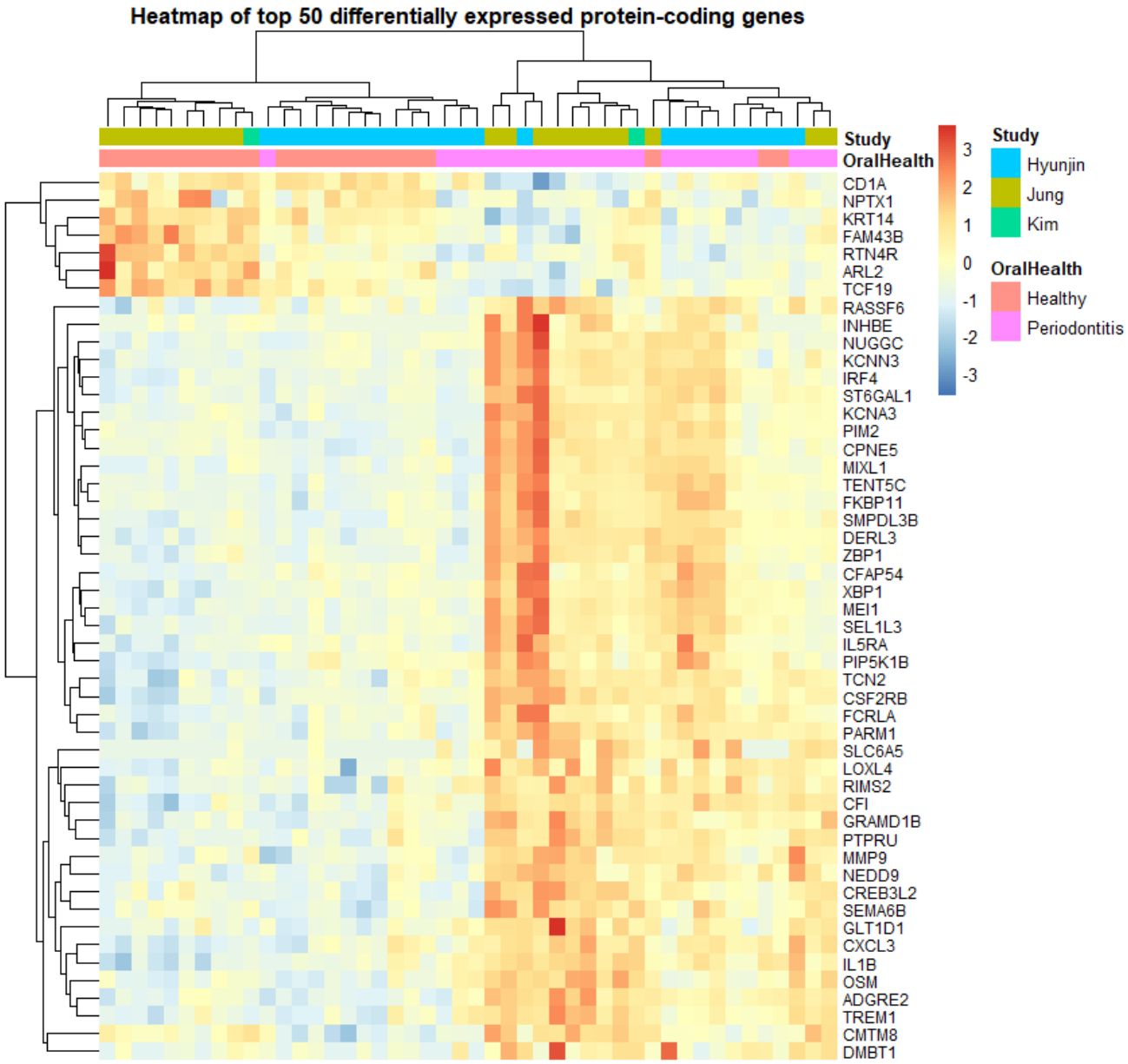


Figure 3 : Heatmap of top 50 DE protein coding genes

moderate and high expression levels. Corresponding MA plots are provided in Supplementary Figure S3 and Figure S4, indicating a balanced and consistent distribution of differentially expressed genes, with clear separation between upregulated and downregulated groups.

Finally, Gene Ontology (GO) enrichment analysis was performed separately for upregulated (Figure 4) and downregulated genes (Figure 5) to identify biological processes overrepresented in each group. This analysis provides insight into the functional roles and pathways associated with the observed transcriptional changes and supports the biological interpretation of the differential expression results. Among the enriched pathways, some of the most significantly upregulated biological processes included the adaptive immune response, positive regulation of cytokine production, and leukocyte-mediated immunity. In contrast, the most downregulated biological processes were primarily associated with epidermis development, skin development, and keratinization.

DISCUSSION

The present study provides a transcriptomic overview of gene expression differences between healthy and periodontitis gingival tissues, supporting the concept that periodontitis is driven by a dysregulated host immune response to microbial challenge (2,6,15). A clear separation between healthy and diseased samples, with consistent clustering patterns, indicates a distinct and reproducible transcriptional signature, in agreement with previous transcriptomic studies (1,2,12,13).

4.1 Immune recruitment and cytokine signaling

A key finding is the upregulation of genes involved in immune signaling and inflammation including INHBE, DMBT1, SLC6A5, DPP10, and MIXL1.

INHBE, a member of the TFG-β superfamily, regulates inflammatory signaling and tissue remodeling (16) and its upregulation reflects activation of pathways associated with chronic inflammation in periodontitis (1,2). Similarly, DMBT1, a pattern recognition molecule involved in innate immune defense, binds bacterial components and indicates an enhanced host response to periodontal pathogens (17). SLC6A5, a glycine transporter primarily associated with neurotransmission, has also been identified in inflammatory conditions and its increased expression may reflect altered cellular signaling and metabolic adaptation within inflamed gingival tissues (18,19). In the same context, DPP10 which modulates ion channels and cellular

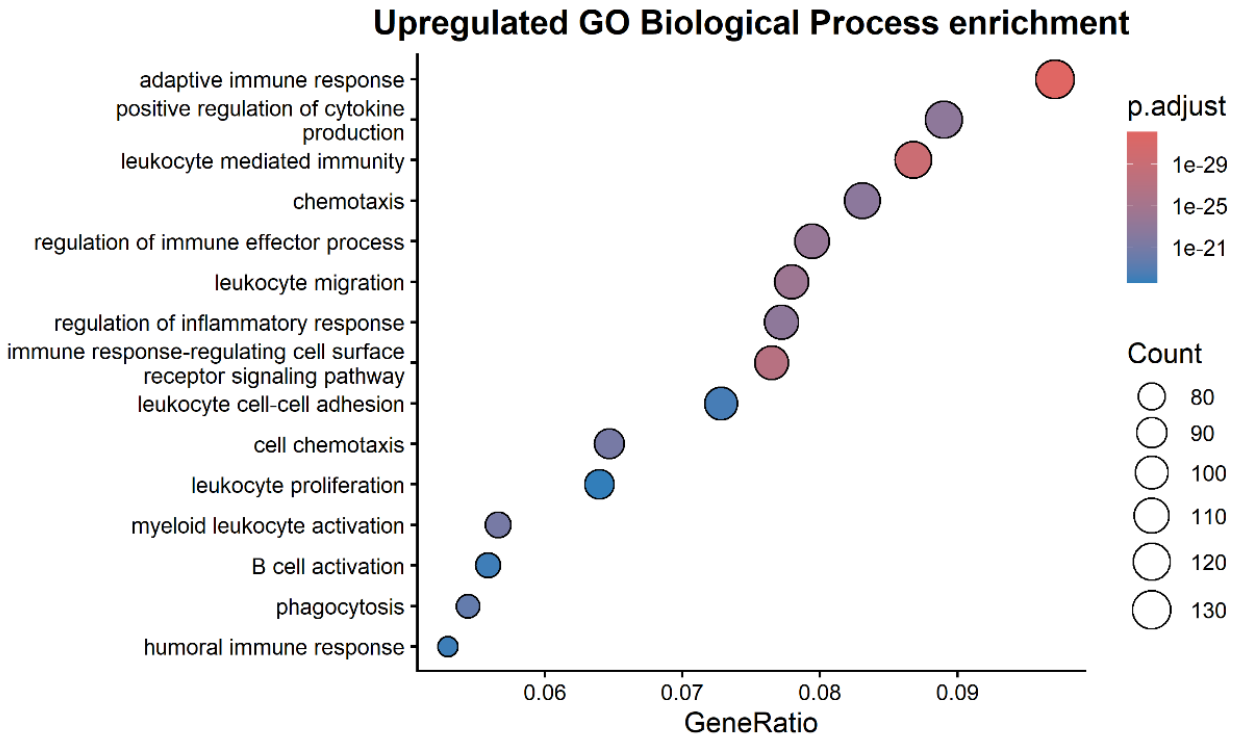


Figure 4 : Upregulated Gene Ontology (GO) biological process enrichment

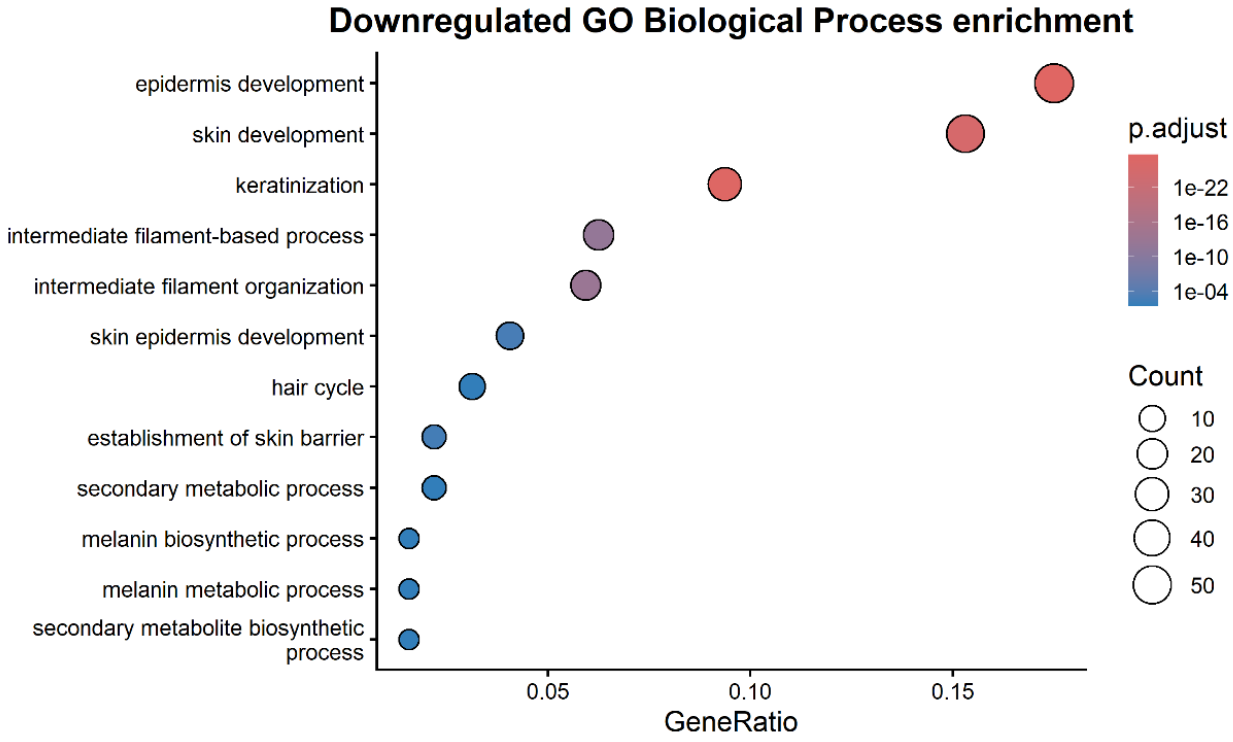


Figure 5 : Downregulated Gene Ontology (GO) biological process enrichment

signaling, may contribute to altered cellular responsiveness in the inflammatory microenvironment (20). Finally, MIXL1, a transcription factor involved in cell differentiation, reflects the activation of transcriptional programs associated with tissue remodeling and immune activity (2,21).

Conversely, downregulated genes, such as SERPINA12, LCE2A, and LCE2C, are associated with tissue homeostasis. SERPINA12 has anti-inflammatory properties and its downregulation may contribute to uncontrolled inflammatory responses (22). LCE2A and LCE2C are part of the late cornified envelope family involved in epithelial barrier formation. Their decreased expression suggests impaired tissue protection and increased susceptibility to bacterial invasion (23).

Together, these findings indicate a shift toward a pro-inflammatory transcriptional profile, with loss of regulatory mechanisms (1,2,15).

At the pathway level, these changes are reflected in the enrichment of the chemokine signaling pathway, with upregulation of key components such as JAK2/3, PI3K, SRC and PLC/PKC, as well as downstream effectors including RAC, WASP, and p47phox. These molecules are involved in signaling cascades that regulate leukocyte activation, cytoskeletal rearrangement and ROS (Reactive Oxygen Species) production, indicating coordinated activation of immune cell migration and inflammatory responses (24–26). The pathway is shown in Supplementary Figure S5.

4.2 Leukocyte migration and cellular adhesion

Periodontitis progression relies on continuous immune cells recruitment, supported by transcriptional changes promoting leukocyte migration(2,15,24).

Among the upregulated genes, DMBT1 contributes indirectly to leukocyte recruitment by enhancing microbial recognition and stimulating local inflammatory responses (17), while INHBE may further regulate immune cell activation and migration through cytokine-mediated mechanisms (16). In parallel, the upregulation of genes involved in signaling and cellular responsiveness, such as DPP10 and SLC6A5, supports the presence of an active communication network between cells, promoting immune cell infiltration and sustaining the inflammatory microenvironment (18,20).

Conversely, several downregulated genes reflect alterations in cellular transport and tissue organization. RAB4B is involved in intracellular vesicle trafficking and receptor recycling, processes that are essential for maintaining cell surface receptor availability, including those

involved in immune signaling (26,27). Its downregulation may impair normal cellular communication and receptor dynamics.

CHRM1, a muscarinic acetylcholine receptor, is involved in cell signaling and regulation of cellular functions, including proliferation and secretion (28). Reduced expression of CHRM1 may indicate disrupted signaling pathways that normally contribute to tissue homeostasis (28).

Additionally, the downregulation of epithelial-related genes such as LCE2A and LCE2C further supports the idea of compromised barrier function, which facilitates leukocyte infiltration and enhances tissue exposure to bacterial products (23).

Overall, these results suggest that leukocyte migration in periodontitis is driven not only by classical inflammatory signals but also by broader alterations in tissue structure, receptor signaling, and cellular communication (15,24,29).

At the pathway level, transepithelial migration involves leukocyte adhesion, cytoskeletal remodeling, and passage across tissue barriers. The upregulation of adhesion molecules (ICAM1, VCAM1), integrins (ITGAL, ITGAM, ITGB2), and chemokine signaling (CXCR4/SDF-1), together with activation of signaling pathways (PI3K, PKC) and cytoskeletal regulators (VAV, Rac2) indicates enhanced leukocyte infiltration, while increased expression of MMPs and reduced epithelial integrity suggest impaired barrier function (15,24–26). The pathway is shown in Supplementary Figure S6.

4.3 Adaptive immunity and B-cell–related expression

Adaptative immunity, particularly B lymphocytes, represents a key component in periodontitis. Lesions are characterized by high infiltration of B cells and plasma cells, contributing to disease progression through antibody and cytokine production (15,30).

Although classical B-cell–specific markers are not among the top five most upregulated genes identified in this study, several of the observed transcriptional changes support an active role of B-cell–mediated immunity. In particular, the upregulation of INHBE suggests activation of cytokine signaling pathways that can influence lymphocyte differentiation and function, including B-cell activation and survival (16). Cytokines from the TGF-β superfamily are known to regulate immune cell proliferation and contribute to the balance between pro-inflammatory and regulatory responses (31).

Furthermore, MIXL1, a transcription factor involved in cellular differentiation, may reflect broader activation of transcriptional programs associated with immune cell expansion and tissue remodeling (21). Although not specific to B cells, its increased expression may indicate an

environment that supports immune cell activation and differentiation within periodontal tissues (15,32).

B lymphocytes in periodontitis are not only involved in antibody production but also play an active role in inflammation. They can produce pro-inflammatory cytokines such as IL-6 and RANKL, which contribute to osteoclast activation and alveolar bone resorption (15,30,33). Additionally, B cells can function as antigen-presenting cells, further amplifying the immune response and sustaining chronic inflammation (15,34).

On the other hand, the downregulation of SERPINA12, a gene with anti-inflammatory properties, suggests a loss of regulatory control over immune responses (22). This may contribute to the persistence of activated B cells and prolonged inflammatory signaling. Similarly, the downregulation of genes involved in cellular signaling and receptor trafficking, such as RAB4B and CHRM1, may impair normal immune regulation and cell–cell communication, potentially affecting B-cell activation and function (26,28).

Overall, these findings support the concept that periodontitis is characterized by a dysregulated adaptive immune response in which B lymphocytes play a central role. This is consistent with previous studies describing enhanced B-cell activity and pro-inflammatory signaling driving chronic inflammation and tissue destruction in periodontitis (15,32,33). Notably, while these results are largely in agreement with existing evidence, some of the highly upregulated genes identified in this study, such as SLC6A5, DPP10 and MXL1, have not been extensively reported in the context of periodontitis (1,2,15). Their differential expression may reflect additional regulatory or metabolic mechanisms contributing to disease progression and highlights potential novel targets for further investigation.

A major strength of this study is the integration of multiple analytical approaches, combined with a relatively large sample size (46 samples, >130 GB of sequencing data), enhancing robustness. However, the use of public datasets introduces heterogeneity and study effect. Additionally, the analysis is limited to transcriptomic data and includes only three studies, which may affect generalizability. Future work should include experimental validation and integration of additional datasets and multi-omics approaches.

5. CONCLUSION

This study successfully characterized the transcriptional profile associated with periodontitis, demonstrating clear differences in gene expression between healthy and diseased gingival

tissues. Differential expression analysis identified numerous significantly altered genes, confirming the rejection of the null hypothesis. Genes related to immune response, cytokine signaling, and leukocyte migration were predominantly upregulated, while genes associated with tissue homeostasis and structural integrity were downregulated. These findings support the presence of a distinct, immune-driven transcriptional profile in periodontitis, consistent with the study objectives.

6. SUSTAINABILITY

This study contributes to sustainability from a social, economic, and environmental perspective, aligning with Sustainable Development Goal 3 (Good Health and Well-being**)**. Periodontitis is a highly prevalent chronic disease with significant impacts on oral and systemic health. By identifying differentially expressed genes and molecular pathways associated with the disease, this work supports the development of earlier diagnostic tools and more targeted therapies. This may improve patient outcomes, reduce disease progression, and decrease the need for invasive and costly treatments, thereby contributing to a more efficient and sustainable healthcare system.

From an environmental perspective, the use of *in silico* analysis and publicly available datasets reduces the need for laboratory experimentation, minimizing the consumption of materials, energy, and biomedical waste. This promotes more sustainable research practices.

Furthermore, integrating transcriptomic data into clinical decision-making may enable personalized dentistry, optimizing treatments and avoiding unnecessary interventions. Future strategies should focus on translating these findings into clinical applications and preventive approaches, contributing to long-term social and economic sustainability in oral healthcare.

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8. ANNEXES

Table S1 : Sequencing data used in the study

ID	Study	Oral Health	ID	Study	Oral Health
SRR23261362	Jung(10)	Healthy	SRR23261352	Jung(10)	Periodontitis
SRR23261363	Jung	Healthy	SRR23261353	Jung	Periodontitis
SRR23261364	Jung	Healthy	SRR23261354	Jung	Periodontitis
SRR23261365	Jung	Healthy	SRR23261355	Jung	Periodontitis
SRR23261366	Jung	Healthy	SRR23261356	Jung	Periodontitis
SRR23261367	Jung	Healthy	SRR23261357	Jung	Periodontitis
SRR23261368	Jung	Healthy	SRR23261358	Jung	Periodontitis
SRR23261369	Jung	Healthy	SRR23261359	Jung	Periodontitis
SRR23261370	Jung	Healthy	SRR23261360	Jung	Periodontitis
SRR23261371	Jung	Healthy	SRR23261361	Jung	Periodontitis
SRR14299217	Hyunjin(11)	Healthy	SRR14299211	Hyunjin(11)	Periodontitis
SRR14299216	Hyunjin	Healthy	SRR14299210	Hyunjin	Periodontitis
SRR14299215	Hyunjin	Healthy	SRR14299209	Hyunjin	Periodontitis
SRR14299214	Hyunjin	Healthy	SRR14299208	Hyunjin	Periodontitis
SRR14299213	Hyunjin	Healthy	SRR14299207	Hyunjin	Periodontitis
SRR14299212	Hyunjin	Healthy	SRR14299206	Hyunjin	Periodontitis
SRR14299199	Hyunjin	Healthy	SRR14299193	Hyunjin	Periodontitis
SRR14299198	Hyunjin	Healthy	SRR14299192	Hyunjin	Periodontitis
SRR14299197	Hyunjin	Healthy	SRR14299191	Hyunjin	Periodontitis
SRR14299196	Hyunjin	Healthy	SRR14299190	Hyunjin	Periodontitis
SRR14299195	Hyunjin	Healthy	SRR14299189	Hyunjin	Periodontitis
SRR14299194	Hyunjin	Healthy	SRR14299188	Hyunjin	Periodontitis
SRR3457548	Kim(12)	Healthy	SRR3457549	Kim(12)	Periodontitis

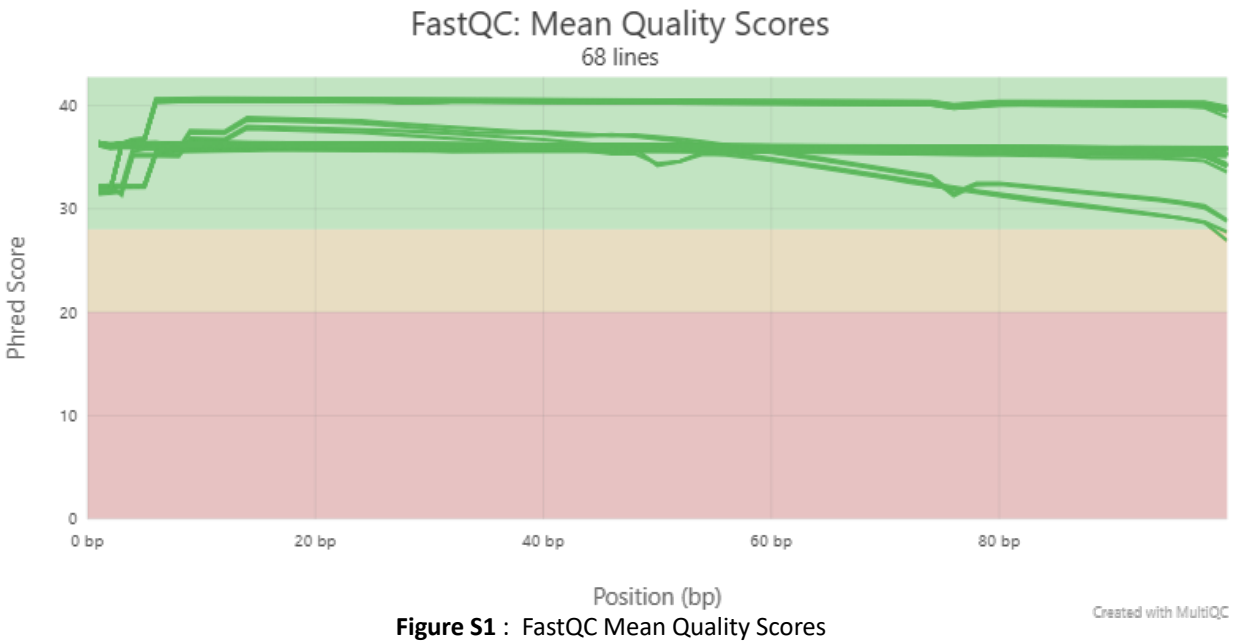


Figure S1 : FastQC Mean Quality Scores

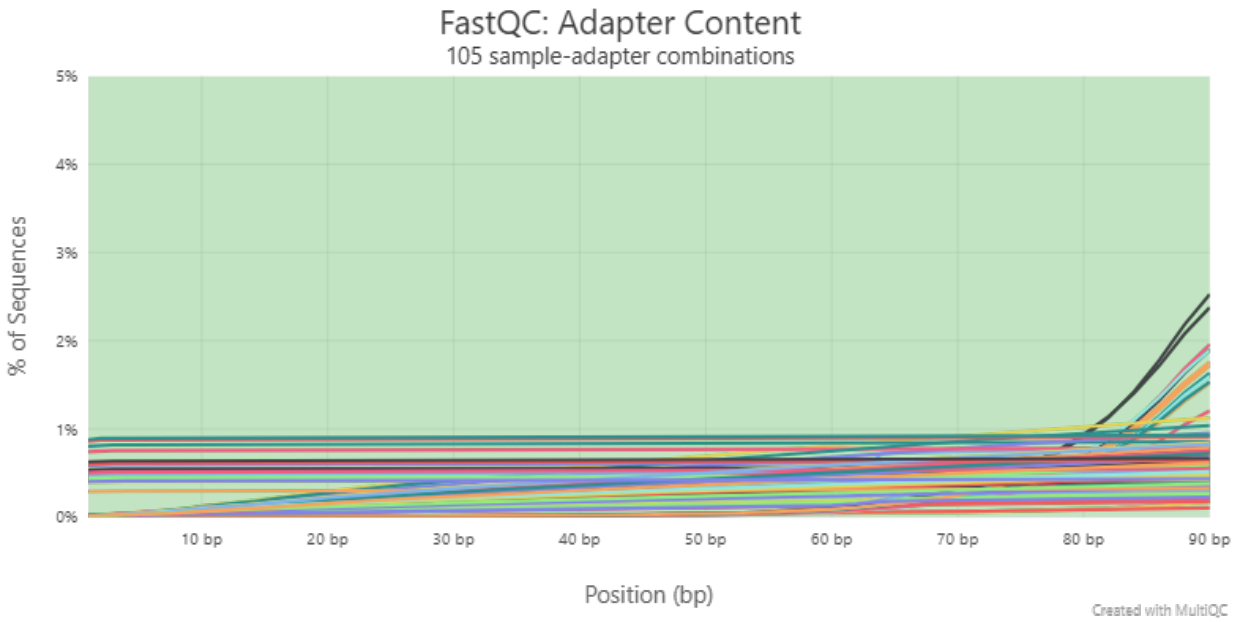


Figure S2 : FastQC Adapter Content

Table S2.1 : 25 most up-regulated genes

Gene_name	GeneID	L2FC	padj
INHBE	ENSG00000139269.4	5,37	2,41E-08
SLC6A5	ENSG00000165970.12	5,01	2,28E-10
DPP10	ENSG00000175497.17	4,34	1,27E-06
DMBT1	ENSG00000187908.21	4,06	3,35E-07
MIXL1	ENSG00000185155.12	3,95	2,68E-07
MZB1	ENSG00000170476.16	3,87	1,88E-06
DCC	ENSG00000187323.13	3,84	1,72E-06
FCRLA	ENSG00000132185.19	3,83	5,81E-09
IGLL5	ENSG00000254709.8	3,77	1,56E-06
AMER2	ENSG00000165566.13	3,69	4,94E-06
JSRP1	ENSG00000167476.11	3,66	5,37E-06
CD79A	ENSG00000105369.10	3,65	6,69E-07
DERL3	ENSG00000099958.16	3,63	6,88E-08
CSF3	ENSG00000108342.14	3,61	5,62E-06
MEI1	ENSG00000167077.14	3,60	2,23E-09
ENSG00000267385	ENSG00000267385.1	3,60	8,70E-07
CHRDL2	ENSG00000054938.17	3,51	5,62E-06
CCL3L3	ENSG00000276085.1	3,49	1,63E-06
BHLHA15	ENSG00000180535.5	3,48	3,62E-06
TNFRSF17	ENSG00000048462.11	3,45	9,08E-06
MMP7	ENSG00000137673.10	3,43	9,45E-06
FCRL5	ENSG00000143297.20	3,43	2,81E-05
NLRP11	ENSG00000179873.14	3,42	4,15E-04
ACOXL	ENSG00000153093.22	3,41	2,65E-05
CST1	ENSG00000170373.9	3,39	4,42E-04

Table S2.2 : 25 most down-regulated genes

gene_name	GeneID	L2FC	padj
ENSG00000267059	ENSG00000267059.2	-5,37	4,30E-04
SERPINA12	ENSG00000165953.11	-3,97	1,97E-05
RAB4B-EGLN2	ENSG00000171570.11	-3,69	1,49E-04
LCE2A	ENSG00000187173.4	-3,35	4,75E-04
CHRM1	ENSG00000168539.5	-3,27	1,82E-05
LCE2C	ENSG00000187180.4	-3,23	2,20E-04
KPLCE	ENSG00000198854.5	-3,21	2,14E-04
CCER2	ENSG00000262484.2	-3,20	1,27E-06
SLC7A13	ENSG00000164893.9	-3,19	5,91E-03
TYR	ENSG00000077498.9	-3,06	7,82E-03
AQP5	ENSG00000161798.8	-3,04	5,37E-05
MLANA	ENSG00000120215.10	-3,04	8,18E-03
LCE2B	ENSG00000159455.9	-3,02	4,29E-04
TOX3	ENSG00000103460.18	-2,91	2,33E-04
PIRT	ENSG00000233670.8	-2,91	7,60E-04
SPINK13	ENSG00000214510.10	-2,72	5,34E-03
PRR9	ENSG00000203783.5	-2,71	4,25E-03
LCE1B	ENSG00000196734.9	-2,67	1,70E-04
LCE6A	ENSG00000235942.3	-2,65	2,01E-03
LORICRIN	ENSG00000203782.6	-2,64	3,41E-04
TMEM271	ENSG00000273238.3	-2,64	8,79E-04
DCT	ENSG00000080166.16	-2,60	2,48E-03
KRT1	ENSG00000167768.4	-2,60	2,25E-04
STAC2	ENSG00000141750.8	-2,54	4,83E-04
NPTX1	ENSG00000171246.7	-2,53	2,60E-07

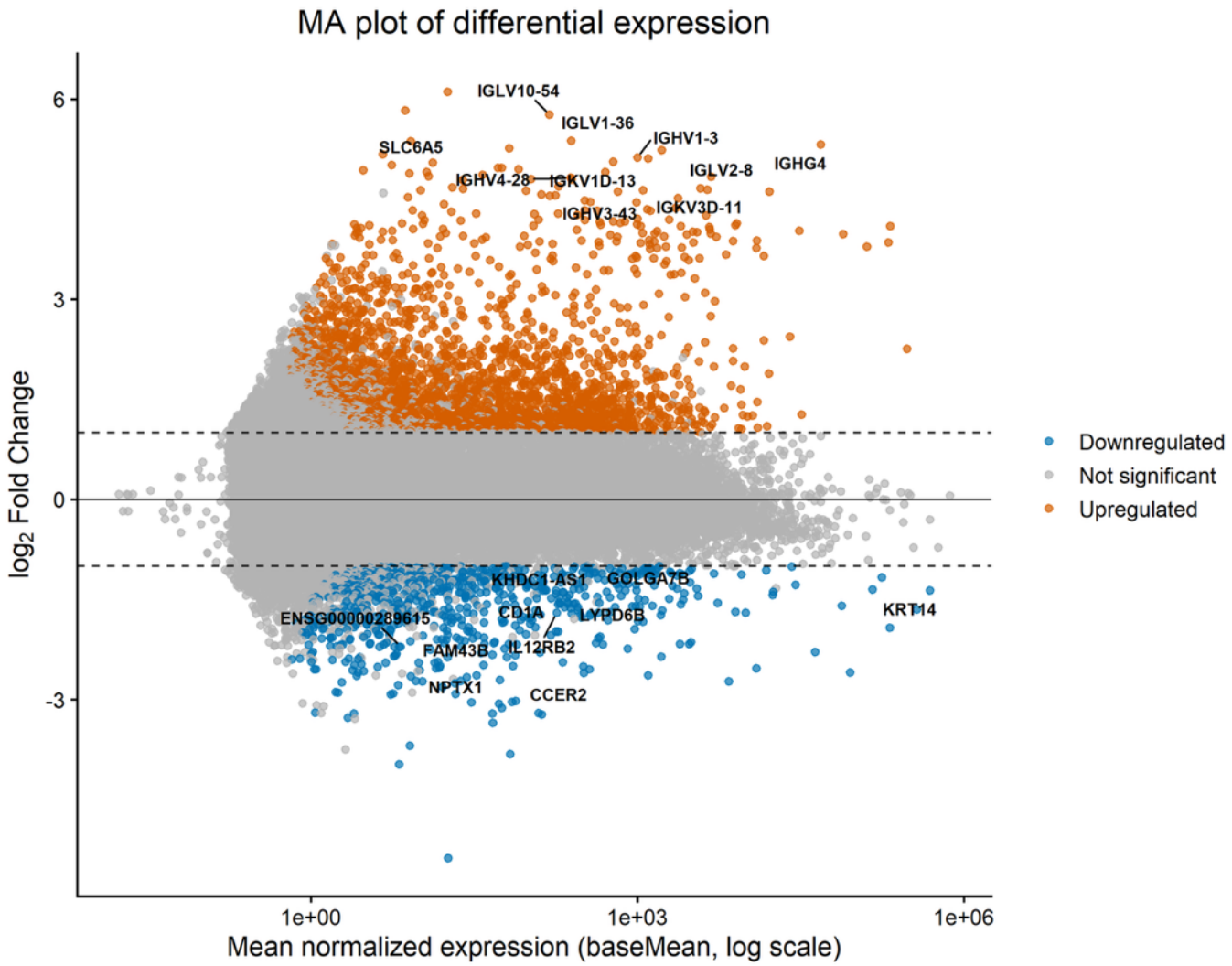


Figure S3 : MA plot of DE genes

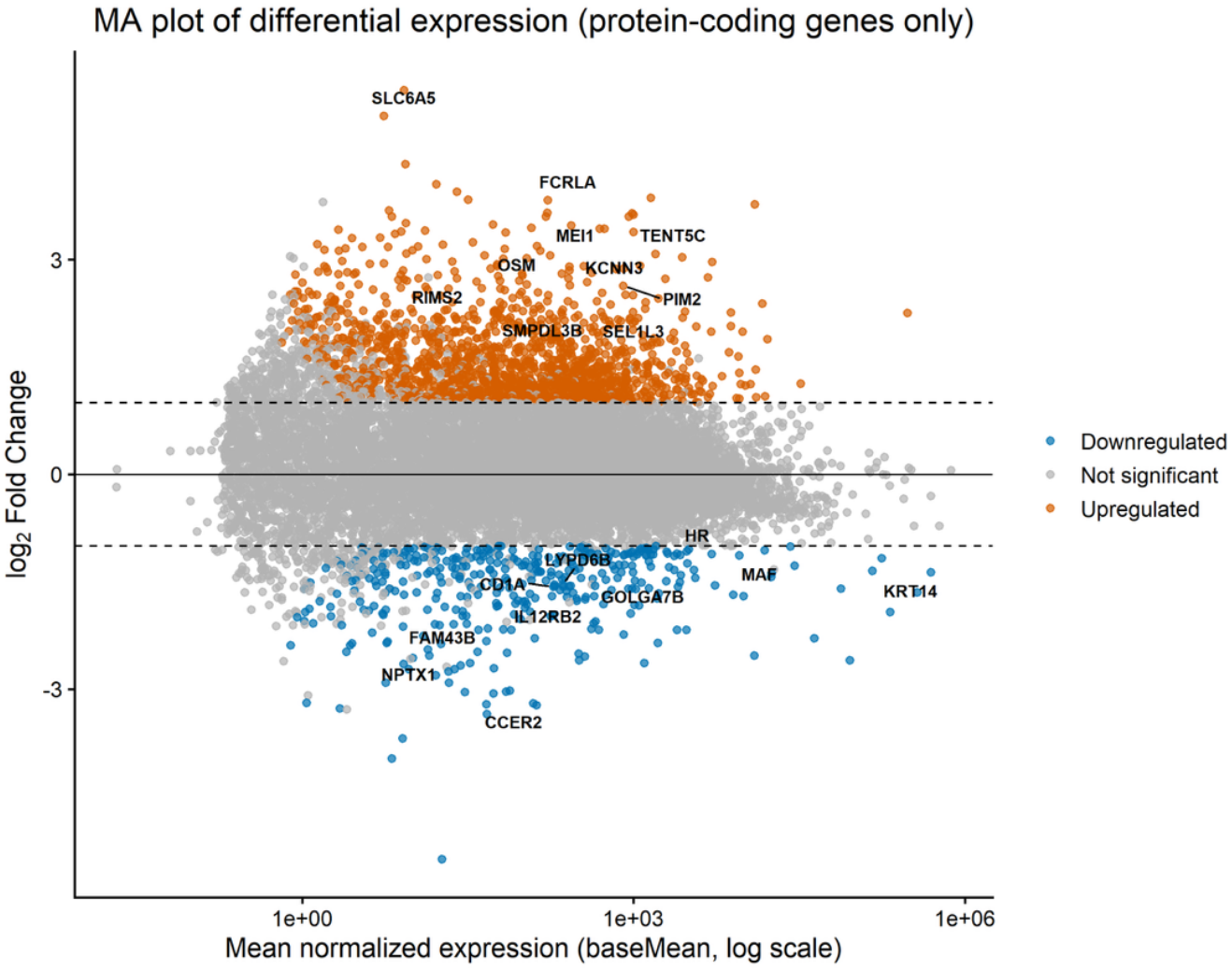


Figure S4 : MA plot of DE (protein coding genes)

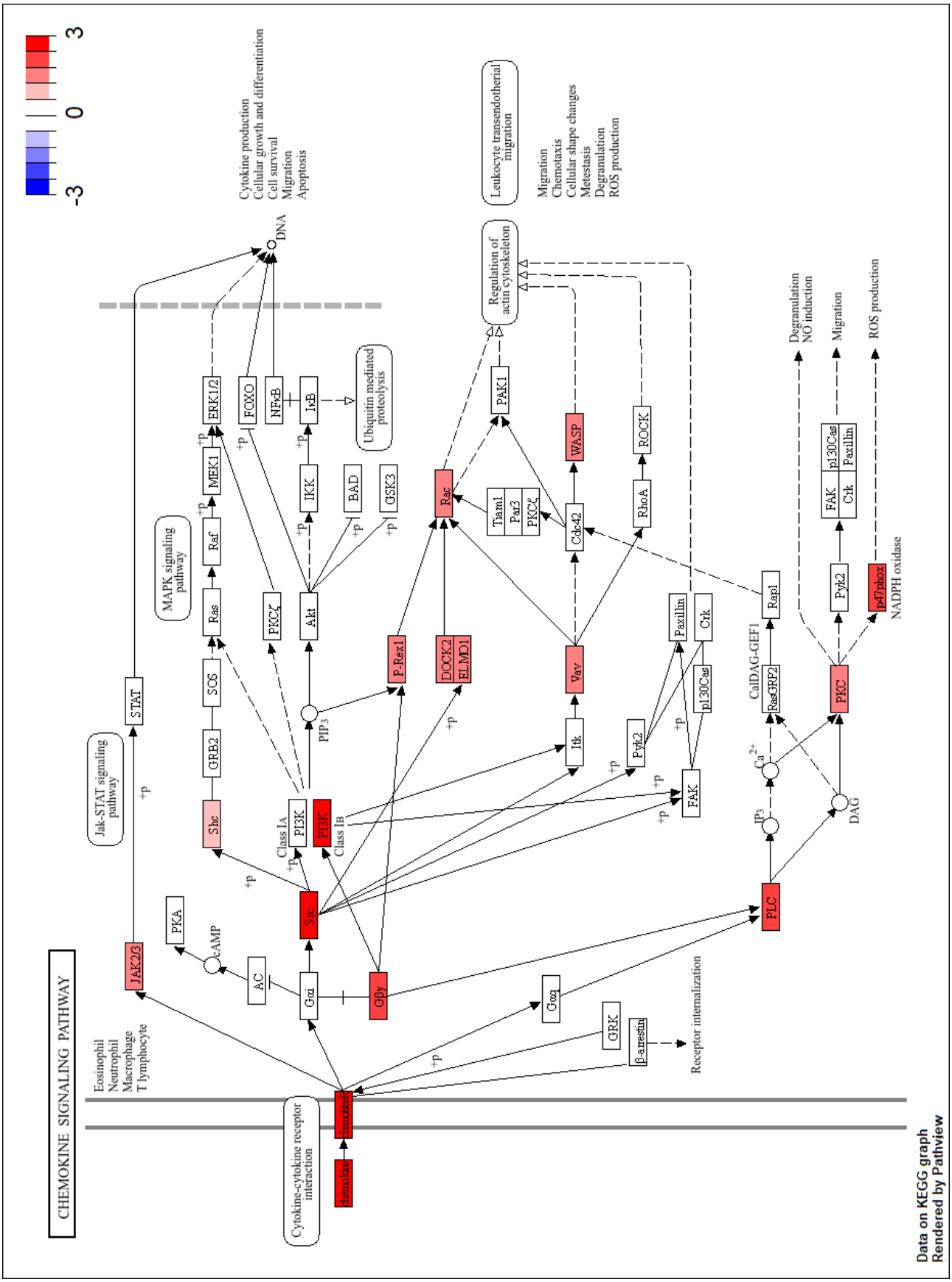


Figure S5 : KEGG : Chemokine signaling pathway

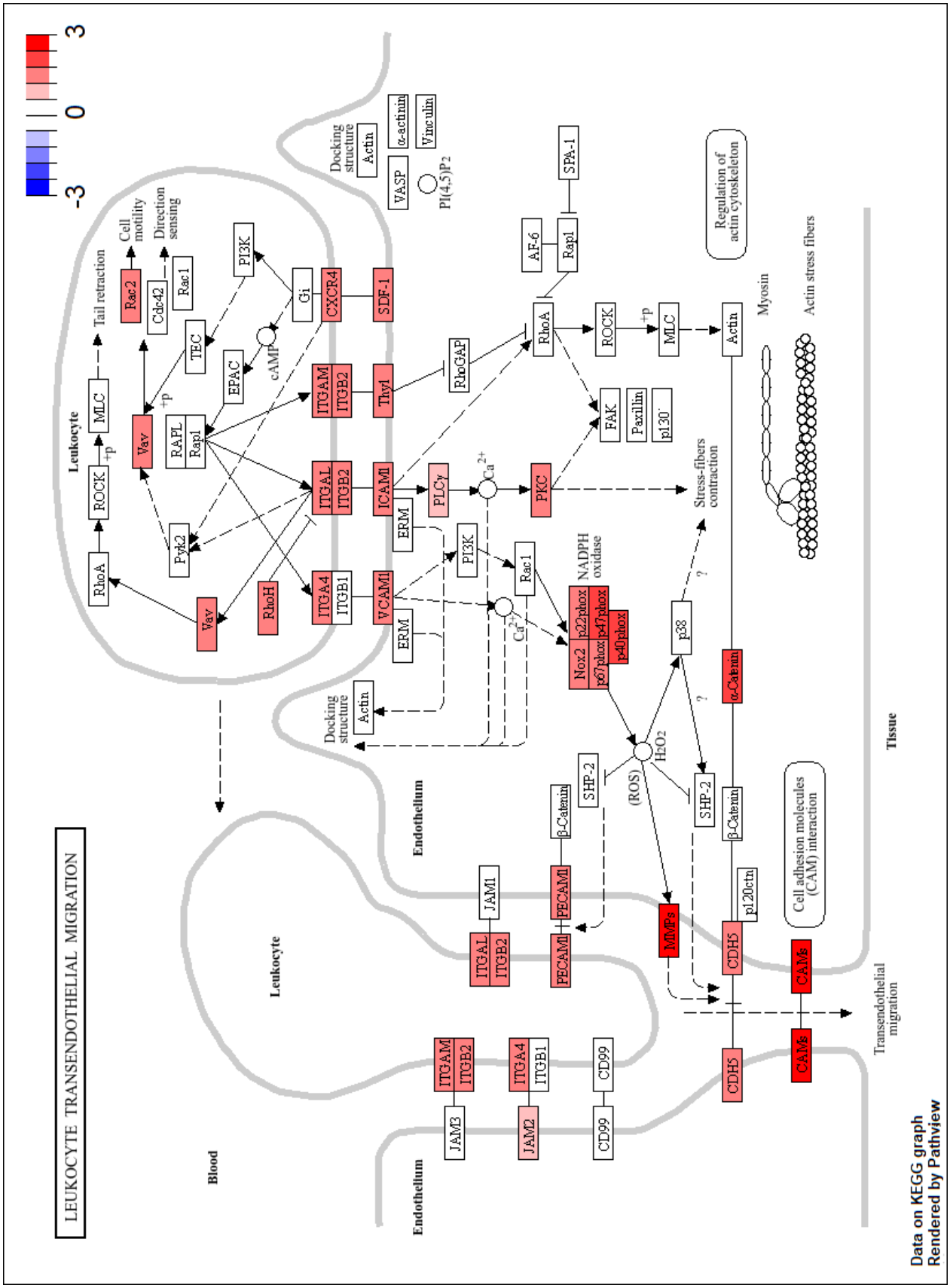


Figure S6 : KEGG : Leukocyte transendothelial migration