Data Article

Gene expression data of inflammatory mediators in apical periodontitis in 129 (wild type) and 5-lipoxygenase knockout mice

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\textbf{ABSTRACT}

Apical periodontitis is an immune inflammatory response around periapical tissues as a result of pathogens invasion into the root canal. The host immunoinflammatory response could determine the progression of this disease, which involves the recruitment of immune cells, and the release of several cytokines in the lesion site. The 5-lipoxygenase pathway has been activated in some osteolytic diseases due to its capacity to interfere in the proliferation and differentiation of bone cells, including the osteoclasts. As mean to understand the inflammatory genes regulation in the apical periodontitis progression, we evaluated the network of 66 genes related to cytokines, chemokines and other inflammatory mediators and receptors in the wild-type (WT) and 5-lipoxygenase enzyme genetically deficient mice (KO). This article presents data not published but related to the research article “Effects of 5-lipoxygenase gene

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disruption on inflammation, osteoclastogenesis and bone resorption in polymicrobial apical periodontitis”.

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Specifications Table

| Subject                                      | Dentistry, Oral Surgery and Medicine |
|----------------------------------------------|-------------------------------------|
| Specific subject area                        | Endodontics                         |
| Type of data                                 | Gene expression (fold change) relative to control |
| How data were acquired                       | RNA extraction followed by reverse transcription |
|                                              | Amplification in qRT-PCR machine (40 cycles) |
|                                              | Instruments: Step one Plus (Applied Biosystems), GeNeCK web server and Software R |
| Data format                                  | Raw, Graphs, Figures, Table in Excel datasheet, Report relative expression, Analyzed |
| Parameters for data collection               | Jaw samples with apical periodontitis and control (contralateral jaw with healthy teeth without lesion) from 5-lipoxygenase enzyme knockout mice and wild-type mice were collected as described [1,2]. Several inflammatory mediators were evaluated by qRT-PCR [1]. |
| Description of data collection              | Inflammatory mediators gene expression array was compared at different time points of apical periodontitis in the 5-lipoxygenase enzyme knockout mice and compared to wild-type mice. |
| Data source location                         | Institution: Universidade de São Paulo |
|                                              | City/Town/Region: Ribeirão Preto |
|                                              | Country: Brazil |
| Data accessibility                           | Full data is host in a public repository. Repository name: Universidade de São Paulo. Direct URL to data: http://repositorio.uspdigital.usp.br/handle/item/336 |
| Related research article                    | Paula-Silva, F., Arnez, M., Petean, L., Almeida-Junior, L. A., da Silva, R., da Silva, L., & Faccioli, L. H. (2020). Effects of 5-lipoxygenase gene disruption on inflammation, osteoclastogenesis and bone resorption in polymicrobial apical periodontitis. Archives of oral biology, 112, 104,670. 10.1016/j.archoralbio.2020.104670 |

Value of the Data

- The data shows a panorama of inflammatory genes profile in the apical periodontitis progression in the wild-type and 5-lipoxygenase enzyme knockout mice.
- This data provides a valuable tool for studying the apical periodontitis development by comparing the inflammatory genes expression modulation in both animals using heatmap and gene regulatory networks in both models.
- The data could contribute to interpretation of 5-lipoxygenase enzyme to the inflammatory genes expression network during the apical periodontitis development.
1. Data Description

The 5-lipoxygenase enzyme deficiency in mice can result in changes in the immunoinflammatory markers gene expression during the apical periodontitis development. Furthermore, the absence of this enzyme affects gene interaction resulting in a broader network at 28 days of the disease. Table 1 integrates symbol and nomenclature of genes evaluated by qRT-PCR. The raw data of qRT-PCR analysis of each gene can be found in the Supplementary file. Fig. 1 shows a heatmap with 66 inflammatory mediator genes evaluated in the apical periodontitis of WT and KO at different stages of the disease, after 7, 14, 21 and 28 days of apical periodontitis. Gene regulatory network was evaluated in wild type (Fig. 2) and in knockout mice (Fig. 3), both at 28 days after apical periodontitis induction. In Figs. 2 and 3, the regulatory genes (Hub gene) and connected genes (nodes genes) of each group were shown.

![Heatmap and cluster analysis of kinetic of 66 genes expression](image)

**Fig. 1.** Heatmap and cluster analysis of kinetic of 66 genes expression in the apical periodontitis of WT and KO mice at 7, 14, 21 and 28 days of lesion and their respective control groups. Color codes in each panel refer to blue for low expression and red for the highest expression levels.
| Unigene   | GeneBank   | Symbol   | Nomenclature                      |
|-----------|------------|----------|-----------------------------------|
| NM_013854 | NM_009744  | Abcf1    | ATP-binding cassette, sub-family F (GCN20), member 1 |
| NM_009778 | NM_098907  | Casp1    | Caspase 1                         |
| NM_011330 | NM_009117  | Ccl11    | Chemokine (C-X-C motif) ligand 11  |
| NM_011331 | NM_011332  | Ccl12    | Chemokine (C-X-C motif) ligand 12  |
| NM_011333 | NM_011334  | Ccl17    | Chemokine (C-X-C motif) ligand 17  |
| NM_011888 | NM_011333  | Ccl19    | Chemokine (C-X-C motif) ligand 19  |
| NM_011330 | NM_011333  | Ccl2     | Chemokine (C-X-C motif) ligand 2   |
| NM_009145  | NM_009960  | Ccl20    | Chemokine (C-X-C motif) ligand 20  |
| NM_009117  | NM_011327  | Ccl22    | Chemokine (C-X-C motif) ligand 22  |
| NM_019577  | NM_009178  | Ccl24    | Chemokine (C-X-C motif) ligand 24  |
| NM_091938  | NM_009138  | Ccl25    | Chemokine (C-X-C motif) ligand 25  |
| NM_013654  | NM_011338  | Ccl7     | Chemokine (C-X-C motif) ligand 7   |
| NM_009912  | NM_011325  | Ccl9     | Chemokine (C-X-C motif) ligand 9   |
| NM_009915  | NM_009912  | Ccr1     | Chemokine (C-C motif) receptor 1   |
| NM_009915  | NM_009915  | Ccr2     | Chemokine (C-C motif) receptor 2   |
| NM_009914  | NM_009914  | Ccr3     | Chemokine (C-C motif) receptor 3   |
| NM_009916  | NM_009916  | Ccr4     | Chemokine (C-C motif) receptor 4   |
| NM_009917  | NM_009917  | Ccr5     | Chemokine (C-C motif) receptor 5   |
| NM_009835  | NM_009835  | Ccr6     | Chemokine (C-C motif) receptor 6   |
| NM_007719  | NM_007719  | Ccr7     | Chemokine (C-C motif) receptor 7   |
| NM_007720  | NM_007720  | Ccr8     | Chemokine (C-C motif) receptor 8   |
| NM_009913  | NM_009913  | Ccr9     | Chemokine (C-C motif) receptor 9   |
| NM_007768  | NM_007768  | Crp      | C-reactive protein, pentraxin-related |
| NM_008176  | NM_008176  | Cxcl1    | Chemokine (C-X-C motif) ligand 1   |
| NM_021704  | NM_011333  | Cxcl2    | Chemokine (C-X-C motif) ligand 12  |
| NM_009936  | NM_011337  | Pf4      | Platelet factor 4                  |
| NM_009910  | NM_009910  | Cxcr3    | Chemokine (C-X-C motif) receptor 3 |
| NM_007721  | NM_007721  | Cxcr10   | Chemokine (C-C motif) receptor 10  |
| NM_008337  | NM_008337  | Ilfg     | Interferon gamma                   |
| NM_008348  | NM_008348  | Il10ra   | Interleukin 10 receptor, alpha     |
| NM_008349  | NM_008349  | Il10rb   | Interleukin 10 receptor, beta      |
| NM_008350  | NM_008350  | Il1l     | Interleukin 11                     |
| NM_133990  | NM_008357  | Il13ra1  | Interleukin 13 receptor, alpha     |
| NM_010551  | NM_010551  | Il14     | Interleukin 15                     |
| NM_019508  | NM_019508  | Il17b    | Interleukin 17B                    |
| NM_008360  | NM_008360  | Il18     | Interleukin 18                     |
| NM_019450  | NM_019450  | Il1f6    | Interleukin 1 family, member 6     |
| NM_027163  | NM_027163  | Il1f8    | Interleukin 1 family, member 8     |
| NM_008362  | NM_008362  | Il1r1    | Interleukin 1 receptor, type I    |
| NM_010555  | NM_010555  | Il1r2    | Interleukin 1 receptor, type II   |
| NM_008368  | NM_008368  | Il2rb    | Interleukin 2 receptor, beta chain |
| NM_013563  | NM_013563  | Il2rg    | Interleukin 2 receptor, gamma chain |
| NM_010556  | NM_010556  | Il3      | Interleukin 3                      |
| NM_021283  | NM_021283  | Il4      | Interleukin 4                      |
| NM_008370  | NM_008370  | Il5ra    | Interleukin 5 receptor, alpha      |
| NM_010559  | NM_010559  | Il6ra    | Interleukin 6 receptor, alpha      |
| NM_008404  | NM_008404  | Il7g2    | Interleukin 7g2                    |
| NM_010735  | NM_010735  | Lta      | Lymphotoxin A                      |
| NM_008518  | NM_008518  | Ltb      | Lymphotoxin B                      |
| NM_009909  | NM_009909  | Cxcr2    | Chemokine (C-X-C motif) receptor 2 |
| NM_007926  | NM_007926  | Aimp1    | Aminocaclyl RNA synthetase complex-interacting |
| NM_009263  | NM_009263  | Spp1     | Multifunctional protein 1          |

(continued on next page)
**Table 1 (continued)**

| Unigene   | GeneBank   | Symbol  | Nomenclature                      |
|-----------|------------|---------|-----------------------------------|
| Mm.248380 | NM_011577  | Tgfb1   | Secreted phosphoprotein 1          |
| Mm.1293   | NM_013693  | Tnf     | Transforming growth factor, beta 1 |
| Mm.474976 | NM_011609  | Tnfrsf1a| Tumor necrosis factor             |
| Mm.235328 | NM_011610  | Tnfrsf1b| Tumor necrosis factor receptor superfamily, member 1a |
| Mm.4861   | NM_011616  | Cd40lg  | Tumor necrosis factor receptor superfamily, member 1b |
| Mm.103551 | NM_023764  | Tollip  | CD40 ligand                       |
| Mm.390241 | NM_011798  | Xcr1    | Toll interacting protein          |
| Mm.3317   | NM_010368  | Gusb    | Chemokine (C motif) receptor 1    |
| Mm.299381 | NM_013556  | Hprt    | Glucuronidase, beta               |
| Mm.2180   | NM_008302  | Hsp90ab1| Hypoxanthine guanine phosphoribosyl transferase |
| Mm.304088 | NM_008084  | Gapdh   | Heat shock protein 90 alpha, class B member 1 |
| Mm.391967 | NM_007393  | Actb    | Glyceraldehyde-3-phosphate dehydrogenase |

**Fig. 2.** Gene regulatory network (GRN) using the Graphical Lasso ($\lambda = 0.300$) method of WT mice at 28 days of lesion. Yellow circles indicate regulatory genes (hub gene) and light blue circles indicate poorly connected genes (nodes genes). There is 1 hub gene: CXCL10 participates in gene regulation and biological processes.
Fig. 3. Gene regulatory network (GRN) using the Graphical Lasso ($\lambda = 0.300$) method of KO mice at 28 days of lesion. Yellow circles indicate regulatory genes (Hub gene) and light blue circles indicate poorly connected genes (nodes genes). There are 5 hub genes: IL-1\(\beta\), IL-3, IL-20, CXCL9 and CCL3 participate in gene regulation and biological processes.

2. Experimental Design, Material and Methods

2.1. Animals

Twenty four knockout (KO) mice for 5-lipoxygenase enzyme (129-Alox5tm1Fun; 129-Alox5-/-; The Jackson Laboratory, Bar Harbor, ME, USA) and 24 wild-type 129 mice for the control group were used in this study. Mice were male and adult (6–8 week-old). For the operative procedures the animals were anesthetized by intraperitoneal injections of ketamine hydrochloride (150 mg/kg, Ketamine 10%, Agener União Química Farmacêutica Nacional S/A, Embu-Guaçu, SP) and xylazine (7.5 mg/kg, Dopaser, Laboratorios Calier S/A, Barcelona, Spain).

2.2. Apical periodontitis model

The protocol of apical periodontitis was previously described in Da Silva et al. [2]. Mice were placed in a surgical table in order to promote the immobilization of the animals, maintenance of the mouth opened, and the visualization of the molar teeth. The upper first molar pulps were exposed using a 1011 spherical diamond tip (KG Sorensen Ind. Com. Ltda., Barueri, SP) and a type K file #06 (Les Fils d’Auguste Maillefer S/A, Switzerland). The exposed root canals were left open to the oral environment, as previously described [3]. The teeth without pulp exposure
were used as controls. Mice were euthanized on days 7, 14, 21 and 28 after experimental apical periodontitis induction ($n = 6$ teeth per period).

2.3. Evaluation of gene expression by global qRT-PCR arrays to demarcation of inflammatory event

A guanidine thiocyanate protocol (RNeasy® Mini, Qiagen Inc., Valencia, USA) was used for RNA extraction from two pools of three teeth each. The evaluation of the total RNA quality was performed by electrophoresis on 1% agarose gel (Sigma-Aldrich Corp.) containing ethidium bromide (Sigma-Aldrich Corp.) using 1x concentrated TBE buffer (Tris-Borate-EDTA). The estimate of the amount of nucleic acids and their purity were assessed by spectrophotometry in NanoDrop 1000 (Thermo Fisher Scientific Inc., Wilmington, USA). The synthesis cDNA via reverse transcription reaction was performed by using 2 μg of total RNA and the First Strand RT² kit (Qiagen Inc.).

RT-PCR arrays (Inflammatory Cytokines and Receptors PAMM-011Z, Qiagen Inc.) were used for the analysis of 66 target sequence genes (Table 1). As reference genes, Gusb, Hprt, Hsp90ab1, Actb and Gapdh were evaluated. Controls for detecting mouse genomic DNA contamination (MGDC), controls for the efficiency of the reverse transcription reaction (RTC) and the positive controls (PPC) consisting of a passive artificial DNA sequence to be detected during the reaction. The qRT-PCR reactions were performed using SybrGreen, consisting of a duplicate in an Eppendorf Mastercycler® ep Realplex (Eppendorf AG). Amplification was done under the following conditions: denaturation at 95 °C for 10 min; followed by 40 cycles of 95 °C for 15 s and 60 °C for 1 min. The specificity of the primers was analyzed using the dissociation curve, considering the melting temperature of the amplicon under the following conditions: temperature increase to 95 °C for 15 s, followed by decrease the temperature to 60 °C for 15 s, gradually increasing the temperature to 95 °C for 20 min and maintained at 95 °C for 15 min. The $\Delta\Delta$Ct method was used for relative quantification.

2.4. Data presentation and analysis

The qRT-PCR data of 66 gene expressions were plotted in MS Excel for the data normalization. The relative quantification of all experimental groups were analyzed by R statistical package version 4.0.3. For data analysis, a heatmap was used in order to show the magnitude of the fold change of each gene in a color scale. The columns correspond to the experimental groups and the rows the genes evaluated.

2.5. Gene regulatory networks

The gene-gene association network of the same 66 genes was evaluated in the WT and KO group, both with 28 days of apical periodontitis, using the Graphical Lasso method ($\lambda = 0.300$) by GeneCK, a web server for building gene networks and visualization [4]. These graphs shows the nodes representing the genes and the edges representing the gene-gene interaction.

Ethics Statement

All experiments using animals were performed following the guidelines for animal research at University of São Paulo (USP). The experimental protocols were approved by the Ethics Committee on Animal Use from the School of Dentistry of Ribeirão Preto (process# 12.1.60.53.8).
Declaration of Competing Interest

The authors declare no conflict of interest for this article.

CRediT Author Statement

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Supplementary Materials

Supplementary material associated with this article can be found in the online version at doi: 10.1016/j.dib.2021.107787.

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