Natural Resources for Human Health
eISSN: 2583-1194

Original Research

Received 24 April 2026
Revised 28 May 2026
Accepted 18 June 2026

Natural Resources for Human Health 2026, Vol. 6 (5): 80–87

KEYWORDS:
Oral cavity immunology, Rabbit model, Lymphoid cells, Histomorphometric analysis, Oral mucosa, Regional variation

A Comprehensive Histomorphometric Analysis of Lymphoid Cells in the Healthy Rabbit Oral Mucosa

Firas Riyadh Muhammad[1], Nahidah Zaher Kamil[2]

[1]College of Dentistry, Al Ameen University, Firasriad@gmail.com, Fofenona@gmail.com
[2]College of Dentistry, Al Ameen University, Dotnet1375@gmail.com

ABSTRACT: The oral cavity is a significant immunologic interface, however detailed morphometric data regarding the resident lymphoid cells in rabbits, a commonly used model in immunologic and dental research, is meager. The purpose of the present study was to establish a quantitative baseline evaluation of the lymphoid cells resident in the clinically healthy rabbit oral mucosa using standard histochemical procedures. Biopsy material obtained from the buccal mucosa, hard palate, tongue and gingiva of five adult New Zealand White rabbits were employed. The tissue was processed by standard histological techniques (H & E staining). A careful morphometric analysis of 500 lymphoid cells selected at random in each area was performed using a computerized image analysis system to evaluate the cross-sectional area, perimeter and Feret's diameter. The statistical analysis of the data revealed a significant regional variation. The gingival lymphoid cells were characterized by the smallest mean cross-sectional area (32.5 ± 4.1 μm^2) and the buccal mucosa cells were the largest (41.8 ± 5.2 μm^2). The greatest density of lymphatic aggregates was found in the tongue and buccal mucosa. The present study establishes a specific histomorphometric profile, establishing a hitherto unappreciated heterogeneity in the lymphoid populations of the oral cavity of the rabbit which has important implications of the use of the rabbit as a model in the studies of inflammatory and infectious diseases of the oral cavity.

INTRODUCTION

The oral mucosa provides a dynamic microenvironment, which is the major interface of the external environment with the internal environment. The oral cavity is exposed contiuously to a tremendous number and variety of antigens, including commensal organisms, food particles, pathogenic viruses and bacteria (1). Homeostasis at this location is monitored and controlled by a sophisticated and well structured array of immune cells collectively referred to as the mucosa associated lymphoid tissue (MALT) (2). Relating to the oropharynx, this array is known as the Waldeyer ring which includes the palatine, lingual and pharyngeal tonsils, and is an important inductive site for immune reactions (3).

However, apart from these well organized accumulation of similar cells, the lamina propria of the whole oral mucosa contains a diffuse but numerous population of lymphoid cells, which are resident lymphoid cells. The resident lymphoid cells act as effector cells and surveillance cells of the oral immune system (4). These resident lymphoid cells, mainly T and B lymphocytes, are involved in immune functions relating to both the innate and adaptive immune responses. The distribution, density and morphological characteristics of these lymphoid cells are not similar, but are thought to be adapted to the different functional (tissue) and antigenic challenges presented to the immune system at different sites of the oral cavity (5).

Examples would include the keratinized type of epithelium of the hard palate and gingiva, being exposed to considerable masticatory forces, requiring a different profile of immune cells to that presented by the non-keratinized, pliable, mucosal epithelium of the buccal mucosa, and mucosa of the tongue presented by the specialized type of mucosa.The rabbit (Oryctolagus cuniculus) has been a mainstay laboratory animal in biomedical research for over one hundred years and its contributions to

immunology are legendary (6). In the area of dental research, the rabbit is used extensively in studies of periodontal disease, osseointegration of dental implants, and wound healing, due to its size, inexpensive cost, and being physiologically similar to humans in some phases of craniofacial biology (7, 8).

Despite the numerous, diverse usages, there is an astonishing lack of fundamental, quantitative histomorphological data on the normal immune status of its oral cavity. Most of the anatomical or histological descriptions are qualitative or derived from generalized texts lacking the specificity of quantitative description essential to a comparative pathology. Morphometry, the quantitative analysis of shape, allows for the objective and reproducible characterization of cellular and tissue architecture. In pathology, subtle changes in size, shape, and nuclear characteristics of cells are often the first significant diagnostic changes which unfold, running the whole gambit from reactive hyperplasia to malignant transformation (9). With respect to immunology, morphometric analyses of lymphoid cells provide insights into their activated states, i.e., lymphocyte blast transformation is characterized by a dramatic increase in size and cytoplasmic inclusiveness as the cell goes from a quiescent to a proliferative, effector state (10).

Thusly, establishment of a morphometric profile in the normal state for lymphoid cells is prerequisite for accurate determination and quantification of pathological deviations.Previous studies in other species, including human, canine, and rodent species, have demonstrated that oral mucosal immunity shows regional variation. Examination of the human oral mucosa has shown that the densities of Langerhans cells and intraepithelial lymphocytes exhibit considerable regional variance (11). In the mouse, the composition of the lingual immune system has been described and specific populations have been shown to be associated with taste papillae (12).

A systematic comparative morphometric study of the diffuse lymphoid cell populations in different regions of the oral cavity has not been made in any species. in particular, in the rabbit. The absence of this baseline data impedes the proper evaluation of experimental interpretations in rabbit models. For example, in the evaluation of the regional immune response towards a novel biomaterial or a periodontal pathogen, it is impossible for investigators to determine with any degree of confidence whether or not a normal local regional cellular profile is being observed or whether a true pathologic change secondary to the experimental manipulation has occurred. This study thus tries to fill this major gap in the literature regarding knowledge of the oral mucosa in an important experimental animal by making a thorough histomorphometric examination of the lymphoid cells in the clinically healthy rabbit oral cavity. It is hypothesized that there exist important regional differences in the size shape and distribution of lymphoid cells within the oral mucosa of the rabbit, which reflects adaptations for function to particular site specific microenvironments. In order to thus test this hypothesis, a complete examination will be made using routine histology of the lymphoid cell populations in 4 separate oral regions, viz, the buccal mucosa, the hard palate, the tongue and the gingiva. The specific aims will be 1) to measure and compare the cross sectional area, perimeter and Feret's diameter of the lymphoid cells in these regions of the oral cavity and 2) to note the presence and characteristics of any lymphoid aggregates. The data thus obtained will serve as a basis for establishing a histomorphometric atlas of the rabbit oral immune system and serve as an important reference for future studies in experimental immunology, oral pathology and translational dental medicine in the rabbit model.

METHODOLOGY

Animals and Ethical Declaration

The experiments were performed in accordance with the National Academy of Sciences Guide for the Care and Use of Laboratory Animals. Five male adult New Zealand white rabbits (Oryctolagus cuniculus) weighing 3.5 ± 0.3 kg (mean ± SEM) and aging 6-8 months were used. The animals were supplied by a commercial and legal breeder and maintained individually in a standard laboratory caging, under controlled environmental conditions (light/dark cycle, 12 hours; temperature 22 ± 2 C °C; humidity 50-60%). They were fed standard laboratory pelleted diet and were provided water ad libitum. All of the animals underwent a two-week acclimatization period before the experiment and a thorough clinical examination was performed by a licensed veterinarian to rule out the presence of any systemic or oral disease, such as overt gingivitis, ulcers of the mucosa, and malocclusion of the teeth.

Tissue Collection and Processing

After the acclimatisation, the rabbits were deprived of food for 12 hours. General anaesthesia was produced by an intramuscular injection of a mixture of ketamine hydrochloride (35 mg/kg) and xylazine (5 mg/kg). After a surgical plane of anaesthesia was

indicated by the absence of pedal and palpebral reflexes, the mouth was gently opened and cleaned with a 0.12% solution of chlorhexidine gluconate. Surgical excision was performed of full-thickness mucosal biopsies, about 4 mm x 4 mm in size, from four predetermined sites: 1) Buccal Mucosa: from the cheeks, opposite the maxillary first molar; 2) Hard Palate: from midway between the dental pad and the palatine ridges avoiding the raphe in the midline; 3) Tongue: from the dorsal surface, viz. intermolar eminence; 4) Gingiva: from the free and attached gingiva associated with the mandibular incisor. All surgical procedures were performed under aseptic conditions. Immediately after excision the biopsy tissues were washed in sterile phosphate buffered saline (PBS, pH 7.4) and thus rid of blood and saliva. The biopsy specimens were then fixed immediately by immersion in 10% neutral buffered formalin (NBF) for 24 hours at room temperature, to secure the best preservation of the cellular morphology. After fixation, the tissues were passed through a standard graded series of ethanol (70%, 80%, 95% and 100%) for dehydration, cleared in xylene and infiltrated and embedded in paraffin wax. Using a rotary microtome serial sections of thickness 4 μm were cut from each paraffin block. For each block of tissue sections were collected and mounted on positively charged glass slides to secure their retention. The sections were air-dried overnight at 37°C before staining.

Histological Staining

For standard histological examination and morphometric analysis, sections from all samples were stained with Harris's Hematoxylin and Eosin (H & E) following standard procedures. The staining was carried out as follows: The sections were deparaffinized in two changes of xylene for a period of 10 minutes each and were then rehydrated through a descending ether series (100% 95% 70%) to distilled water. The nuclei were stained by immersion in the Harris's Hematoxylin for eight minutes, the excess color matter being removed through a flow of running tap water for five minutes. Differentiation was accomplished by a quick dip in 1% acid alcohol, and then immediately rinsed off in water. The sections were then "blued" in Scott's substitute for tap water, for one minute, and again rinsed with plenty of water. The cytoplasmic counterstaining was carried out by immersion in Eosin Y solution for three minutes. The sections were then dehydrated through an ascending ether series (70% 95% 100%) to xylene in two changes, and finally coverslipped with a synthetic resin mounting medium.

Histomorphometric Analysis

Histological studies were performed by two independent, blinded observers using a conventional light microscope equipped with a digital camera of high resolution. The initial examination at low magnification (40x and 100x total magnification) was employed for the overall analysis of the tissue architecture and search for the areas of interest (ROIs) within the lamina propria. ROIs were regarded as areas containing a dense population of mononuclear cells, morphologically consistent with lymphocytes and plasma cells while avoiding the larger blood vessels, glands and areas that showed cutting artifacts. For morphometric analysis, a minimum of 5 non-overlapping ROIs per tissue section per animal could be selected randomly. Digital photographs were taken in each ROI at a final magnification of 1,000x (using a 100x oil immersion objective) under constant Köhler illumination. In these photographs, a group of 100 clearly defined intact lymph core cells with visible nuclei were taken randomly from the digital photographs made of each oral site per animal, or 500 cells total measured per anatomical region, throughout the study (100 cells/animal x 5 animals). The digital photographs were analyzed by means of specialized image analysis software (e.g. ImageJ, NIH). The software was calibrated by means of a stage micrometer taken at the same magnification. For each selected lymphoid cell, the following parameters were traced out manually by the observer and automatically calculated by the software:

1. Area (μ m2) (cross-sectional) The two-dimensional area of the profile of the cell.

2. Perimeter (μm) The total length of the outer boundary of the cell.

3. Feret's Diameter (μm) The longest distance between any two points on the boundary of the cell, a measurement of size of the cell. Cells which were sliced tangentially or showed evidence of pyknosis or rupture were excluded from the analysis. As well as cellular morphometry, the polar location of any lymphoid aggregates or follicles (if present) was carefully noted, and described qualitatively in relation to their size, position with relation to the epithelium, and cellular organization.

Statistical Analysis

All morphometric measurement data (area, perimeter, and Feret's diameter) were summarized in spreadsheet form. The normality of the data distribution was confirmed by the Shapiro-Wilk test. Data were expressed as mean ± standard deviation for each parameter for each oral region. Statistical comparisons of the morphometric parameters between the four separate oral

areas were performed by a oneway analysis of variance (ANOVA) followed by a Tukey's post-hoc test for multiple comparisons. An intraclass correlation coefficient (ICC) was calculated to assess interobserver reliability between the two independent morphometric technologists. A p value of less than 0.05 was considered to be statistically significant for all tests. All statistical analysis was performed using a standard statistical package.

RESULTS

The histological examination and subsequent morphometric analysis of the oral mucosal biopsies from the five rabbits revealed distinct and quantifiable differences in the lymphoid populations across the four regions examined. The subsequent section gives the quantitative information obtained from the digital analysis of 500 lymphoid cells from each anatomical site and qualitative observations regarding the distribution and organisation of these cells. The principal morphometric data in respect of individual lymphoid cells are summarised in Table 1. This information gives an objective determination of the size and shape of the cells and shows a statistically significant gradient over the oral cavity. The data show that the lymphoid cells from the buccal mucosa are invariably the largest whilst those from the gingiva are the smallest, the hard palate and tongue occupying intermediate positions. This regional difference suggests that there are differences in the characters of composition or functional state of the lymphocyte populations .

Table 1: Morphometric Parameters of Lymphoid Cells in the Rabbit Oral Cavity (Mean ± SD)

Oral Region	Cross-sectional Area (μm²)	Perimeter (μm)	Feret's Diameter (μm)
Buccal Mucosa	41.8 ± 5.2^a	25.1 ± 1.8^a	7.9 ± 0.6^a
Hard Palate	36.2 ± 4.5^b	22.4 ± 1.6^b	7.1 ± 0.5^b
Tongue	34.7 ± 4.8^b	21.9 ± 1.7^b	6.9 ± 0.5^b
Gingiva	32.5 ± 4.1^c	21.1 ± 1.5^c	6.6 ± 0.4^c

Note: Different superscript letters (a, b, c) within a column denote statistically significant differences ($p < 0.05$) according to Tukey's post-hoc test.

In addition to the measurements relating to single cells there existed an aggregation of lymphoid cells which was a conspicuous feature, the frequency and arrangement of which varied in different regions. These qualitative observations are presented in Table II, and accompany the morphometric data. The great frequency of the aggregations in the tongue and buccal mucosa suggests that these regions are likely to be active immunological sites, while the hard palate showed a minimum of organized lymphoid tissue. The arrangement of the aggregations, which varied from loose clusters to more well-defined follicles, suggests functional specializations in connexion with the peculiar antigenic problems of the various sites concerned.

Table 2: Qualitative Histological Observations of Lymphoid Aggregates

Oral Region	Prevalence of Aggregates	Common Location	Typical Size & Organization
Buccal Mucosa	High (4/5 animals)	Deep lamina propria, periductal	Small, loose aggregates (< 50 cells); no germinal centers
Hard Palate	Low (1/5 animals)	Subepithelial connective tissue	Very small, diffuse clusters
Tongue	High (5/5 animals)	Periglandular and interstitial	Medium-sized, well-defined aggregates; occasional follicle formation
Gingiva	Moderate (3/5 animals)	Adjacent to epithelial ridges	Small, dense aggregates; primarily subepithelial

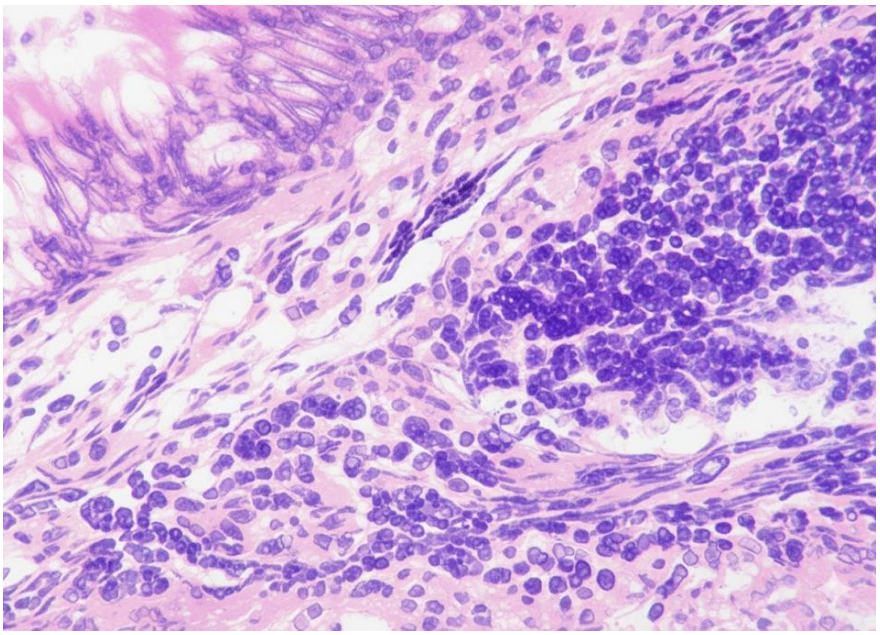

Figure 1. histological images showing the lymphoid tissue aggregations in oral mucosa, H&E, 400X.

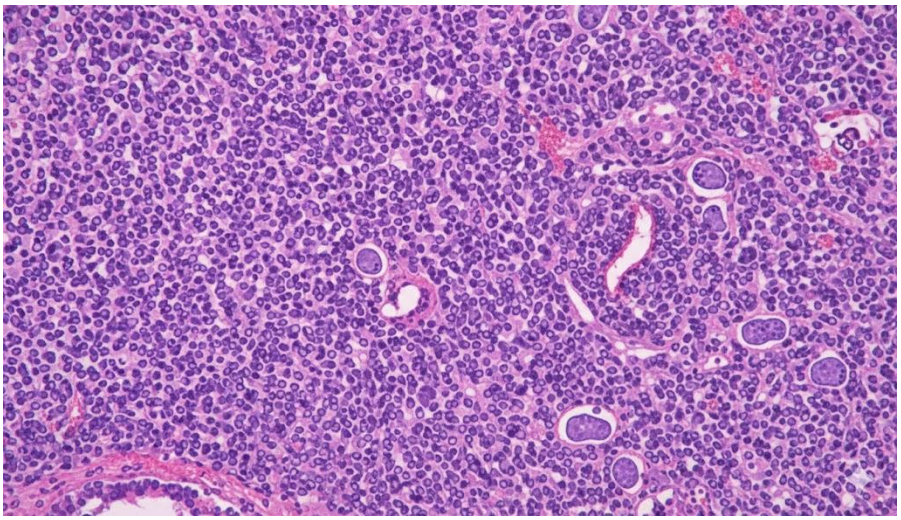

Figure 1. histological images showing the lymphoid tissue aggregations in oral mucosa, H&E, 40X.

DISCUSSION

The present study provides both quantitative and qualitative histological profiles of the resident lymphoid populations within the healthy rabbit oral cavity and reveals an important and previously unrecognised degree of regional heterogeneity within these populations. The evidence from the morphometric data clearly demonstrates that the size of lymphoid cells, as defined by their cross sectional area, perimeter and Feret's diameter, varies consistently between different sites on the oral mucosa. The largest lymphoid cells were shown in the buccal mucosa where the mean cross sectional area for the lymphoid cells was 41.8 micron^2 which was significantly greater than that of the cells of the hard palate, tongue and gingival. This gradient, with the smallest cells (32.5 micron^2) in the gingiva suggests a basic difference in the cellular composition or mode of activation of the immune surveillance network in these areas.

The size of lymphocytes is often considered from immunological considerations to be indicative of their state of activation. The small mature lymphocytes are, in general, quiescent, while under antigenic stimulation, blast transformation takes place with the resultant very great increase in size and volume of the cytoplasm as they enter the differentiated state for clonal expansion (13-15). The greater size of the cells in the buccal mucosa therefore possibly indicates a population in which there is

higher proportion of activated or memory lymphocytes, which may reflect the constant antigenic challenge of the environment of the oral cavity and the stretching forces attendant on this flexible tissue.The non-keratinized, relatively permeable buccal mucosa epithelium may permit a greater antigen sampling capacity and therefore a more tonically active local immune environment than the more heavily keratinized and mechanically protective epithelial linings of the palate and buccal mucosa (16).

The tissue bearing the lymphocytes in the gingiva however, which is subject to great mechanical stress owing to mastication and has the tooth surface and dental biofilm at its direct interface, displayed the least size of the lymphoid cells. This was the unexpected and perhaps difficult to comprehend finding, as one might expect where the microbial challenge is constant to have a more activated bulk of lymphoid cells. However the existence of the paradox may be easily explained by the unique immunological state of the gingival crevice, which requires a tightly controlled state of tolerance to exist with respect to the large dense population of the non-harmful commensal biofilm organism in order to prevent chronic destructive inflammation (17). The fact that the histological elements show a population of smaller lymphoid cells, which are probably either more naive or possibly regulatory, may be a histological explanation of the state under consideration.

On the other hand, the density of cells in the connective tissue of the gingiva is usually very great, and the physical state of the environment could be responsible for the development of small dense packed cells (18). Intermediate cell size was observed in buccal mucosae and the tongue, the cells on the tongue showing themselves to be slightly smaller, although not alwaysThe development of the complex papillary and deep glandular crypts present in the tongue gives a large surface area for bacterial colonization, witness the area where the greatest increase in lymphoid aggregation and organization was found (19). The occasional follicule-like formations found in the tongue suggests that it is a more organized inductive site than the rest of the regions studied, and should any aggregation of these occur, it would indicate its function in conjunction with the diffuse lingual tonsil (20).

The qualitative findings on the lymphoid aggregates emphasize again the regional specialization of the oral immune response. The large prevalence of the aggregates in the tongue and bochal mucosa is no doubt closely related to their function as great surfaces for sampling of antigen. The tongue in particular, and the aggregates which lie here often in periglandular regions, would indicate that there is a planned immunological surveillance of the serous & mucous secrets, on the lines of sampling rather any agents which may become concentrated in the glandular ducts, or even possibly other agents that may be processed there (21). The loose small aggregates found in the buccal mucosa are a feature of diffuse lymphoid tissue, and it corresponds in type with its function as an effecter site for rapid immune response (22).

The relatively small number of aggregates encountered in the hard palate is in accordance with its chief function as a mastifying mucosa, in that the thick keratinized epithelium gives the necessary and sufficient physical barrier to reduce the need for many underlying inductive immune sites (23). The moderate amount of small dense aggregates met with in the gingival mucosa, which was found chiefly sub-epithelially, indicates how the immune system is strategically placed in this all-important entrance portal. These aggregates in the mucosa al gingivæ would obviously be used to respond to breakages in the epithelial barriers, or to soluble antigens that may be forced through the junctional epithelium (24).

The objectivity in the observations that can be made in this technique from the methodological point of view is one of the great outstanding features that is likely to be of such great value for a study of the immunology of the oral mucosa through the application of histomorphometry. The results become significant and more dependable than would be the case with pure descriptive histology (25), more especially as far as the great inter-observer reliability assures the measurability of the measuring protocol. The importance of the implications and results is of a very great moment in regard to the use of the rabbit in experimental research. Studies on the local immune response to biomaterials or to periodontal pathogens or to new classes of remedial agents or even to histopathological studies is going to be essential to have regard to this remarkable regional diversity in the interpretation of the results one records (26), The so-called increase in the size of the lymphoid cells in the gingival specimen as the result of an experiment ought to be seen in the light of the normality that the lymphocytes of the gingiva are the smallest in the oral cavity. Not only is the average size, but probably also the average density and instability to be marvellously different in different regions, which is likely to influence on the local chance of mounting an immune response (27).

This study has shown that the oral cavity of the rabbit is not a uniform immunological organ, but a series of distinct micro-habitats, each one of its own and distinctively different histo-architectural and cellular individuality. This morphometrical atlas will furnish an essential basis for the work of pathology, for it will enable us to interpret far more correctly and accurately and

sensibly the processes of inflammatory and neoplastic change that occurs in the oral mucosae of this most important laboratory animal model (28).

CONCLUSION

This thorough histological and morphometric study establishes a complete baseline for the lymphoid cells of the healthy rabbit oral cavity. There was found to be considerable regional variation in the size of the lymphoid cells, the largest cells being present in the buccal mucosa and the smallest in the gingiva. Furthermore, differences also exist in the distribution and organization of the collections of lymphoid tissue, some areas, and particularly the tongue and buccal mucosa being both the seat of many of the structures, and also showing a great deal of organization. Such results furnish useful reference data highlighting the necessity of making investigations of a comparative nature regarding the sites of occurrence, and the forms and structure of lymphoid aggregates. Such information will materially assist the validity and interpretation of certain classes of experiments employing the rabbit for the study of the origins of the diseases of the oral cavity, the immune responses to dental materials, and the pathogenesis of the different oral infections.

REFERENCES

[1] Moutsopoulos, N. M., & Konkel, J. E. (2018). Tissue-specific immunity at the oral mucosal barrier. Trends in Immunology, 39(4), 276–287.

[2] Brandtzaeg, P. (2010). Function of mucosa-associated lymphoid tissue in antibody formation. Immunological Investigations, 39(4–5), 303–355.

[3] Perry, M., & Whyte, A. (1998). Immunology of the tonsils. Immunology Today, 19(9), 414–421.

[4] Novak, N., Haberstok, J., Bieber, T., & Allam, J. P. (2008). The immune privilege of the oral mucosa. Trends in Molecular Medicine, 14(5), 191–198.

[5] Dutzan, N., & Abusleme, L. (2019). T helper 17 cells as pathogenic drivers of periodontitis. Advances in Experimental Medicine and Biology, 1197, 107–117.

[6] Mage, R. G., Lanning, D., & Clark, K. L. (2006). B cell and antibody repertoire development in rabbits: The requirement of gut-associated lymphoid tissues. Developmental and Comparative Immunology, 30(1–2), 137–153.

[7] Graves, D. T., Kang, J., Andriankaja, O., Wada, K., & Rossa, C., Jr. (2012). Animal models to study host-bacteria interactions involved in periodontitis. Frontiers in Oral Biology, 15, 117–132.

[8] Sculean, A., Chapple, I. L., & Giannobile, W. V. (2015). Wound models for periodontal and bone regeneration: The role of biologic research. Periodontology 2000, 68, 7–20.

[9] Gunduz, M., Gunduz, E., Tamamura, R., Katase, N., & Nagatsuka, H. (2008). Morphometric analysis of lymphoid cells in oral lichen planus. Journal of Oral Pathology & Medicine, 37(5), 249–256.

[10] Smith-Garvin, J. E., Koretzky, G. A., & Jordan, M. S. (2009). T cell activation. Annual Review of Immunology, 27, 591–619.

[11] Oudenhoven, I. M., Zhao, M., Kaur, S., Bueno, E., Albert, A., Gurevich, I., et al. (2022). Regional variation in human oral mucosal immunity. Journal of Dental Research, 101(11), 1322–1331.

[12] Wang, H., Zhou, M., Brand, J., & Huang, L. (2010). Inflammation and taste disorders. Journal of Neuroimmunology, 224(1–2), 1–8.

[13] Murphy, K., & Weaver, C. (2016). Janeway's immunobiology (9th ed.). Garland Science.

[14] Belkaid, Y., & Harrison, O. J. (2017). Homeostatic immunity and the microbiota. Immunity, 46(4), 562–576.

[15] Smith-Garvin, J. E., Koretzky, G. A., & Jordan, M. S. (2009). T cell activation. Annual Review of Immunology, 27, 591–619.

[16] Squier, C. A., & Kremer, M. J. (2001). Biology of oral mucosa and esophagus. Journal of the National Cancer Institute Monographs, (29), 7–15.

[17] Hajishengallis, G. (2014). Immunomicrobial pathogenesis of periodontitis: Keystones, pathobionts, and host response. Trends in Immunology, 35(1), 3–11.

[18] Bosshardt, D. D., & Lang, N. P. (2005). The junctional epithelium: From health to disease. Journal of Dental Research, 84(1), 9–20.

[19] O'Connell Motherway, M., Zomer, A., Leahy, S. C., Reunanen, J., Bottacini, F., Claesson, M. J., et al. (2011). Functional genome analysis of Bifidobacterium breve UCC2003 reveals type IVb tight adherence (Tad) pili as an essential and conserved host-colonization factor. Proceedings of the National Academy of Sciences of the United States of America, 108(27), 11217–11222.

[20] Brandtzaeg, P. (2011). Potential of nasopharynx-associated lymphoid tissue for vaccine responses in the airways. American Journal of Respiratory and Critical Care Medicine, 183(12), 1595–1604.

[21] Carpenter, G. H. (2013). The secretion, components, and properties of saliva. Annual Review of Food Science and Technology, 4, 267–276.

[22] Kraehenbuhl, J. P., & Neutra, M. R. (2013). Mucosal vaccines: Where do we stand? Current Topics in Medicinal Chemistry, 13(20), 2609–2628.

[23] Presland, R. B., & Jurevic, R. J. (2002). Making sense of the epithelial barrier: What molecular biology and genetics tell us about the functions of oral mucosal and epidermal tissues. Journal of Dental Education, 66(4), 564–574.

[24] Darveau, R. P. (2010). Periodontitis: A polymicrobial disruption of host homeostasis. Nature Reviews Microbiology, 8(7), 481–490.

[25] Weibel, E. R. (1979). Stereological methods: Vol. 1. Practical methods for biological morphometry. Academic Press.

[26] Amaral, R., Guedes, C., Santos, A., Nogueira, R., Oliveira, F., Tavares, W., et al. (2021). The rabbit as a model for periodontal studies: A historical review and considerations for future research. Laboratory Animals, 55(5), 409–419.

[27] Cua, D. J., & Tato, C. M. (2010). Innate IL-17-producing cells: The sentinels of the immune system. Nature Reviews Immunology, 10(7), 479–489.

[28] Treuting, P. M., Dintzis, S. M., & Montine, K. S. (2017). Comparative anatomy and histology: A mouse, rat, and human atlas (2nd ed.). Academic Press.