




# The peri-implant ligament: a scoping review

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The peri-implant ligament is formed from the interface of bone tissue, through the anchoring of proteins and the surface of the dental implant. In this sense, it is relevant to understand the extent to which this ligament is structured and biomimics the periodontal ligament functions. **Aim:** The goal of this scoping review is to present and analyze the peri-implant ligament composition and compare the extent to which this ligament is structured and biomimics the periodontal ligament functions. **Methods:** This scoping review was performed according to the Joanna Briggs Institute methodology for scoping reviews and following the Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for scoping review. Two independent researchers searched Pubmed, Cochrane, Embase, Virtual Health Library, Scielo, Scopus, Web of Science, Brazilian Bibliography of Dentistry, Latin American and Caribbean Literature in Health Sciences, Digital Library of Theses and Dissertations from the University of São Paulo and Portal Capes. Studies published in English, Portuguese and Spanish, over the last 21 years (2000-2021). **Results:** A total of 330 titles were identified and after applying inclusion and exclusion factors, 27 studies were included in this review. All proteins were identified regarding their tissue function and classified into 6 major protein groups. After that this new protein ligament was compared with the periodontal ligament regarding its function and composition. The main proteins associated with osseointegration, and thus, with the peri-implant ligament are recognized as belonging to the periodontal ligament. **Conclusion:** This scoping review results suggest evidence of the composition and function of the peri-implant ligament. However, variations may still exist due to the existence of several modulants of the osseointegration process.

**Keywords:** Osseointegration. Dental implants. Biocompatible materials. Proteins.

## Background

The peri-implant ligament can be described as an osteoconductive proteinaceous ligament that will support the osteoconduction space during the osseointegration process. This ligament will mediate the interactions between bone tissue cells, and thus, osteoblasts with the implanted biomaterial, and more specifically, a relationship between the alveolar periosteum and the osseointegrable dental implant<sup>1,2</sup>.

However, it is noteworthy that the osseointegration process will only occur from a periodontal health status and excellent biocompatibility. Generally, this biocompatibility has been achieved from titanium implants and their alloys, such as titanium commercially pure grade IV, titanium-aluminum-vanadium, titanium-zirconia and even zirconia implants have proven to be a successful replacement<sup>1-3</sup>.

These osseointegrable implants will allow osteoinduction and provide the process of bone formation and remodeling from the protein's adsorption on the topographic implant surface. Thus, there is no direct contact between the bone tissue and the dental implant, but an interface mediated by the anchoring of cellular proteins and the implants' surface<sup>4</sup>.

To the best of our knowledge, there is still no consensus as to the proteins participating in this bone-integration process to the point of constituting a peri-implant ligament. Therefore, the purpose of this scoping review is to present and analyze the peri-implant ligament composition and compare the extent to which this ligament is structured and biomimics the periodontal ligament functions.

## Materials and Methods

This scoping review was performed following the Joanna Briggs Institute methodology for scoping reviews<sup>5</sup> and Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for Scoping Review (PRISMA-ScR)<sup>6</sup> flow diagram. Furthermore, the protocol for this review was registered and submitted to the Open Science Framework (OSF) platform (DOI 10.17605/OSF.IO/9SD5H) and the statistical results were done with Microsoft Excel and Orange 3.30.1

### Review Question

- To what extent can the peri-implant ligament mimic the composition and functions of the periodontal ligament?

### Selection of Studies

The PCC method was used (Table 1). Studies that met the following inclusion criteria were included in this review: osseointegrable dental implants; protein/protein adsorption within the osseointegration process. The study exclusion criteria were as follows: address some pathology; systemic health changes; smoking; grafts; bruxism; orthodontics; periodontitis.

**Table 1.** Election Criteria with the PCC Method

Participants	Concept	Context
Osseointegrable implants and Dental implants. Exclusion criteria: non-dental and non-osseointegrable implants.	Peri-implant ligament and protein adsorption on the implant surface.	Biocompatibility (not foreign body response) and periodontal health (not periodontal disease).

## Search Strategy and Data Extraction

The search was performed on databases: Pubmed (MEDLINE), Cochrane CENTRAL, Embase, Virtual Health Library (VHL), Scielo, Scopus and Web of Science (WoS), and in gray literature: Brazilian Bibliography of Dentistry (BBD), Latin American and Caribbean Literature in Health Sciences (LILACS), Digital Library of Theses and Dissertations from the University of São Paulo (USP Theses) and Portal Capes. The search strategy was performed by two independent researchers and adapted for each database (Table 2). Thus, studies in English, Portuguese and Spanish will be included due to the potential for international access and also those published since the last 21 years (2000-2021) as a consideration of new concepts in modern literature.

Therefore, after searching the literature, duplicate articles were removed. Then, the titles and abstracts were selected by two independent reviewers for evaluation against the inclusion criteria for the review. The full text of selected citations was evaluated in detail against inclusion criteria by two independent reviewers. Reasons for excluding sources of evidence in the full text that do not meet the inclusion criteria will be recorded and reported in the scoping review. Any disagreements that arose between reviewers at each stage of the selection process were resolved through discussion or with an additional reviewer.

**Table 2.** Methodology and Search Key by Digital Platform

Data Base	Search Key	Inclusion Criteria	Exclusion Criteria
Pubmed	((("biomaterials"[All Fields]) AND ("dental implants"[All Fields])) AND ("osseointegration"[All Fields])) AND ("proteins"[All Fields])	Full texts, Portuguese, English and Spanish, in the last 21 years (2000-2021)	non-dental implants; non-osseointegrated implants; cancer
Cochrane	"osseointegration" AND "dental implants" AND "proteins"	Full texts, Portuguese, English and Spanish, in the last 21 years (2000-2021)	articles not available; non-dental implants; articles that do not address protein adsorption
Embase	osseointegration AND 'osseointegrated implant' AND protein	Full texts, Portuguese, English and Spanish, in the last 21 years (2000-2021)	non-dental implants; non-osseointegrated implants; cancer
VHL	(osseointegração) AND (implantes dentários) AND (adsorção de proteínas) AND (year_cluster:[2000 TO 2021])	Full texts, Portuguese, English and Spanish, in the last 21 years (2000-2021)	articles that do not address protein adsorption
Scielo	(osseointegração) AND (protein)	Full texts, Portuguese, English and Spanish, in the last 21 years (2000-2021)	did not answer the question

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Scopus	(TITLE-ABS-KEY ( osseointegration ) AND TITLE-ABS-KEY (dental AND implants ) AND TITLE-ABS-KEY ( protein ) AND TITLE-ABS-KEY ( adsorption AND of AND proteins ) )	Full texts, Portuguese, English and Spanish, in the last 21 years (2000-2021)	non-dental implants; non-osseointegrated implants;
WoS	TÓPICO: (osseointegration) AND TÓPICO: (biomaterials) AND TÓPICO: (dental implants) AND TÓPICO: (protein) AND TÓPICO: (adsorption of proteis)	Full texts, Portuguese, English and Spanish, in the last 21 years (2000-2021)	non-dental implants; non-osseointegrated implants;
BBD	(osseointegração) AND (adsorção de proteínas) AND (year_cluster:[2000 TO 2021])	Full texts, Portuguese, English and Spanish, in the last 21 years (2000-2021)	articles not available
LILACS	osseointegração AND proteínas AND ( db:("LILACS")) AND (year_cluster:[2000 TO 2021])	Full texts, Portuguese, English and Spanish, in the last 21 years (2000-2021)	articles not available; articles that do not address protein adsorption
USP	osseointegração AND implantes AND adsorção de proteínas	Full texts, Portuguese, English and Spanish, in the last 21 years (2000-2021)	non-dental implants; non-osseointegrated implants;
Portal Capes	osseointegration AND protein AND (adsorption of proteins) AND dental implants	Full texts, Portuguese, English and Spanish, in the last 21 years (2000-2021)	non-dental implants; non-osseointegrated implants; articles that do not address protein adsorption; duplicate articles

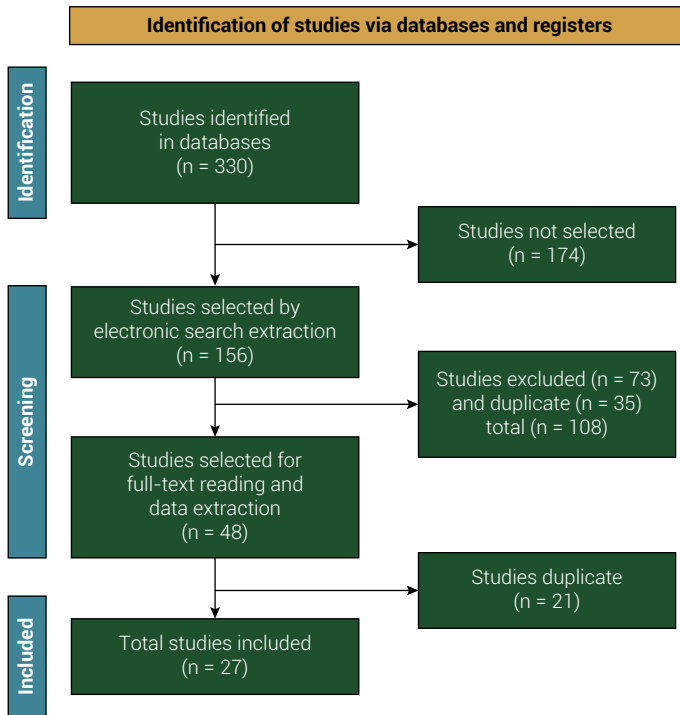
## Statistical Analysis

All protein-related parameters were considered as results for the distribution of proteins into classes. Average and standard deviation (SD) values were estimated from sample size, average mean, average's distance, average's square and variance. The average sum among (between), within (in), and total was also used. In the results, 95% confidence level (CI) was considered. The chi-square test was performed to associate the data distribution with distribution relationship and protein association. The significance level for chi-square was set at 0.05. To evaluate the useful hypotheses comparing this distribution the T-test was performed. The significance level for the T-test was set to 0.05.

## Results

A total of 330 articles were identified during the search. After screening with the reading of the title and abstract, 156 articles remained, then 48 articles were selected to be read in its entirety, and after applying the inclusion and exclusion criteria, in addition to the exclusion of repeated articles, 27 articles were selected. Among the excluded articles, the main reasons were papers that did not answer the question, dropped the subject or even addressed it, but the content did not approach the issue of interest. The selected articles were based, mainly, on proteins that appeared in

osseointegration, either through research of tests with implants, or that addressed this information in the body of the article (Figure 1).



**Figure 1.** Study Selection Flowchart

The studies included in this scoping review are summarized in Table 3. Most of the results did not specify which implant they were based on. The implants described were: commercially pure grade IV titanium (Ti<sub>cp</sub>), titanium-aluminum-vanadium (Ti-6Al-4V), titanium-zirconia (Ti-ZrO<sub>2</sub>), titanium-zirconia-tantalum (Ti-ZrO<sub>2</sub>-Ta), titanium-zirconia-tantalum-nitrogen-sulfur (Ti-ZrO<sub>2</sub>-Ta-N-S), Ti-machined and Ti-sandblasted and etched. These studies provide data for a total of 87 proteins (sum total of 167 proteins) that were classified into seven protein classes: cell membrane, complement system, cytoskeleton, extracellular matrix, factors, plasma, saliva (Figure 2).

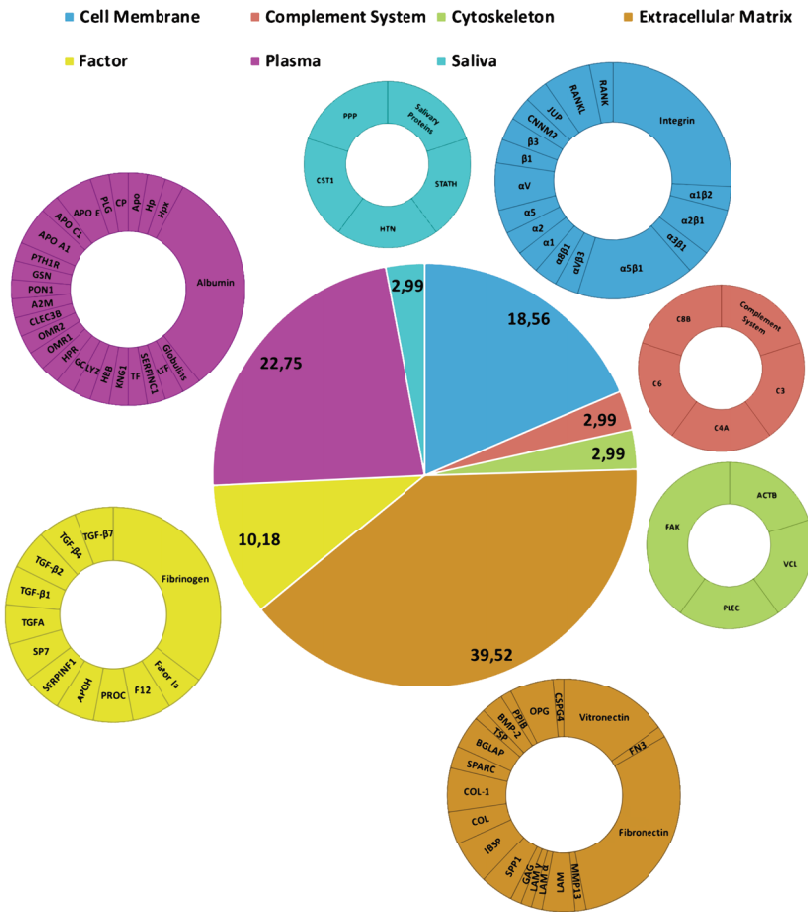


Figure 2. Osseointegration Proteins Statistical Distribution. Distribution of proteins in the seven protein classes (%), chi-square test, p < 0.05.

Table 3. Relation of Proteins in the 27 studies

Reference (Author and Year)	Implants Considered	Related Proteins in the Osseointegration Process
Barberi and Spriano, 2021 <sup>7</sup>	Ticp; Ti-6Al-4V;	Integrin (α <sub>5</sub> β <sub>1</sub> ); Fibronectin; Vitronectin; Bone Morphogenic Protein-2; Fibrinogen; Albumin; Laminin α; Lactoferrin; Collagen type I; Salivary Proteins;
Meyer et al., 2004 <sup>8</sup>	not specified	Fibronectin; Vitronectin; Osteonectin;
Romero-Gavilán et al., 2017 <sup>9</sup>	Ti machined; Ti sandblasted and acid etching;	Integrin α <sub>v</sub> ; Vitronectin; Beta-2-Glycoprotein 1; Complement System (C3; C4α; C6; C8β); CNNM2 metal conveyor; Junction Plakoglobin; Serum Paraoxonase/Arylesterase 1; Plasminogen; Coagulation Factor XII; Gelsolin; Alpha-2-Macroglobulin; Tetranectin; Pigment Epithelium-Derived Factor; Alpha-1-acid glycoprotein (1; 2) Apolipoproteins (ApoA1; ApoC1; ApoE); Proteoglycan 4; Peptidyl-prolyl Cis-Trans Isomerase β; Haptoglobin-Related Protein; Vitamin D Binding Protein; Cytoplasmic Actin 1; Lysozyme C; Hemoglobin β Subunit; Kininogen-1; Serotransferrin; Ceruloplasmin; Plectin; Antithrombin III; Vitamin K Dependent Protein;

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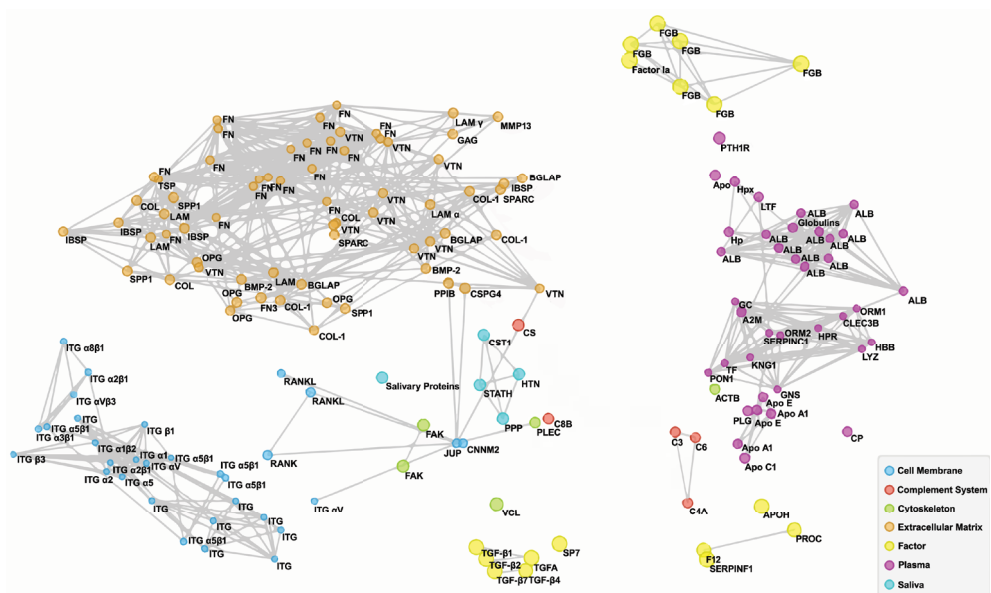
Martínez-Ibáñez et al., 2018 <sup>10</sup>	Ti machined;	Fibronectin; Fibrinogen; Albumin; Collagen type I;
Prati et al., 2013 <sup>11</sup>	not specified	Osteoprotegerin; Osteocalcin; Osteopontin; Parathyroid Hormone; Transforming Growth Factor $\alpha$ ;
Cei et al., 2015 <sup>12</sup>	not specified	Integrin; Fibronectin; Vitronectin; Albumin; Collagen type I;
Matsumoto et al., 2020 <sup>13</sup>	not specified	Fibronectin; Albumin;
Parisi et al., 2020 <sup>14</sup>	not specified	Fibronectin; Albumin;
Wu et al., 2020 <sup>15</sup>	Ti-ZiO <sub>2</sub> ; Ti-ZiO <sub>2</sub> -Ta; Ti-ZiO <sub>2</sub> -Ta-NS;	Albumin; Osteocalcin; Osterix; Osteoprotegerin; OSX; OPG; Receptor Activator of Nuclear Factor Kappa B Ligand; Receptor Activator of Nuclear Factor Kappa B;
Parisi et al., 2019 <sup>16</sup>	not specified	Fibronectin; Vitronectin; Vinculin;
Dayan et al., 2019 <sup>17</sup>	not specified	Integrin;
Subramani et al., 2019 <sup>18</sup>	not specified	Integrin; Fibronectin; Vitronectin; Focal Adhesions;
Boyan et al., 2017 <sup>19</sup>	Ticp; Ti-6Al-4V; Ti-ZiO <sub>2</sub> ;	Integrin ( $\alpha_5\beta_1$ ; $\alpha_2\beta_1$ ; $\alpha_1\beta_2$ ; $\alpha_1$ ; $\alpha_2$ ; $\alpha_5$ ; $\alpha_v$ ; $\beta_1$ ; $\beta_3$ ); Fibronectin; Collagen type 1; Osteoprotegerin; Receptor Activator of Nuclear Factor Kappa B Ligand; Transforming Growth Factor $\beta$ (1; 2; 4; 7);
Cho et al., 2016 <sup>20</sup>	not specified	Integrin ( $\alpha_5\beta_1$ ); Fibronectin type III;
Chen et al., 2014 <sup>21</sup>	not specified	Integrin; Fibronectin; Fibrinogen; Laminin; Bone Morphogenic Protein-2; Osteogenic Growth (OGP);
Lee and Ogawa, 2012 <sup>22</sup>	not specified	Fibronectin; Albumin
Hori et al., 2010 <sup>23</sup>	not specified	Integrin; Fibronectin; Albumin;
Lavenus et al., 2010 <sup>24</sup>	not specified	Integrin; Fibronectin; Vitronectin; Albumin; Focal Adhesions;
Hori et al., 2009 <sup>25</sup>	not specified	Fibronectin; Collagen; Albumin;
Rupp et al., 2018 <sup>26</sup>	not specified	Fibronectin; Vitronectin;
Broggini et al., 2012 <sup>27</sup>	not specified	Integrin; Fibronectin; Vitronectin; Collagen; Laminin; Fibrin; Bone Sialoprotein; Osteopontin; Thrombospondin;
Jaiswal et al., 2019 <sup>28</sup>	not specified	Albumin; Fibrinogen; Globulins; Bone Sialoprotein; Osteocalcin; Osteonectin;
Kopf et al., 2015 <sup>29</sup>	Ticp; Ti-ZiO <sub>2</sub> ;	Fibronectin; Fibrinogen;
Rapuano et al., 2012 <sup>30</sup>	Ticp; Ti-6Al-4V;	Fibronectin; Bone Sialoprotein; Integrin $\alpha_5\beta_1$ ;
Petrie et al., 2009 <sup>31</sup>	not specified	Integrin ( $\alpha_5\beta_1$ ; $\alpha_v\beta_3$ ; $\alpha_3\beta_1$ ; $\alpha_8\beta_1$ ; $\alpha_2\beta_1$ ); Fibronectin; Laminin; Collagen; Bone Sialoprotein; Osteopontin;
Salvoni, 2006 <sup>32</sup>	not specified	Integrin;
Wei et al., 2020 <sup>33</sup>	Ti;ZiO <sub>2</sub>	Fibronectin; Vitronectin; Albumin; Laminin $\gamma$ ; Fibrinogen; Glycosaminoglycans; Collagenase; Apolipoprotein; Complement System Proteins; Phosphopeptides; Haptoglobin; Hemopexin; Salivary Cystatin; Histatin; Statherin;

In the cell membrane, proteins showed the highest percentage rate, 83,91%, being the most prevalent  $\alpha_5\beta_1$  (16,13%),  $\alpha_2\beta_1$  (6,45%),  $\alpha_v$  subunit (6,45%) and an integrin groups could not be classified at the subunit level (25,81%). In the extracellular matrix had a higher abundance of fibronectins (31,82%), being that of fibronectins type III (1,52%), vitronectin (15,15%), collagenous fibers (10,61%), which 6,06% represented type I,

laminin (7,59%), these 1,52% represented the  $\alpha$  and  $\gamma$  subunits (each), osteoprotegerin (6,06%), and bone sialoprotein-2 (6,06%). In the factors group, the most abundant was fibrinogen (35,29%) followed by transforming growth factor (29,4%), with 5,88% for factors  $\alpha$ ,  $\beta_1$ ,  $\beta_2$ ,  $\beta_4$ ,  $\beta_7$  (each). In plasma albumin was the most abundant protein (31,58%) followed by apolipoprotein (13,15%), with the C1 subunit being 2,63% and 5,26% the A1 and E subunits (each).

## Protein Data

All the protein groups will participate at different times in the osseointegration process. In the first moment after implant installation, there will occur the protein adsorption of blood plasma and factors (mediating the angiogenesis process), complement system and almost at the same time salivary proteins. After osteoconduction, the recognition and interaction between osteoblasts and implant will be mediated by cell membrane proteins, cytoskeleton, and bone formation and remodeling by the extracellular matrix bone proteins. Figure 3 shows the proteins network distribution in the osseointegrated process.



**Figure 3.** Multidimensional Protein Scaling. Multidimensional scaling projecting the proteins on adjusted plane representing the distances between points. t-test,  $p < 0.05$ .

## Discussion

The present study explored the proteins involved during the osseointegration process of osseointegrable implants. Several proteins have been previously reported with greater frequency, but the idealization of periodontal ligament regeneration has always been denied. Therefore, this study sought to think about how each protein and protein grouping would behave during the integration process. Con-



sidering the existence of a peri-implant ligament, we decided to investigate to what extent this ligament biomimics the functions of the periodontal ligament. Thus, we hypothetically considered osseointegration compatible with the state of periodontal health.

Osseointegrable implants cannot be in direct contact with bone tissue, since this would not fulfill the tertiary stability function, which is related to the dissipation of these loads after osseointegration, which would result in bone fracture. Thus, the idea that there is a protein ligament around the implant becomes more accepted from this perspective.

Thus, based on agreements and disagreements with the studies in this review, we reached a hypothesis and can make the following consideration: the two ligaments have practically the same composition.

Although the periodontal ligament is described predominantly with Sharpey's fibers that are permeated by collagenous fibers type III, this type of collagenous fiber is not often found alone because it is more fragile (thin), so it is a supportive collagenous fiber that in most cases is accompanied by collagenous fibers type I. In addition, the periodontal ligament contains several collagenous fibers types, such as type I, III, V, VI, XII<sup>34</sup>.

The periodontal ligament cellular components are 50-60% fibroblasts, immune system defense cells, osteoblasts and osteoclasts (hard blade residents), cementoblasts, stem and progenitor cells. Protein components of the extracellular bone matrix such as collagen fibers type I, BMP-2, TFG- $\beta$ , osteocalcin, osteopontin, osteonectin, bone sialoprotein, fibronectin, and proteoglycans are also present<sup>35</sup>.

The periodontal ligament in anatomical classification is described as a gonphous joint and, although it is described as a joint, there are no significant levels of cartilaginous tissue in this region, even though our research found chondroitin sulfate proteoglycan 4 (CSPG4) which is produced by chondroblasts and has the function of lubricating the medium<sup>36</sup>.

Furthermore, the periodontal ligament itself does not have the same nourishing function as the tooth, since the periodontal space is composed of an unformed dense connective tissue with the presence of blood vessels and nerve plexuses. Thus, the tooth is nourished through diffusion determined by the concentration of gradient driving force. This ligament has both sensory and support functions. The first is related to the perception of the tooth in the body, and the second to the support and dissipation of masticatory loads. And these two functions are compatible with the functions of the peri-implant ligament.

In this sense, starting from osteoblasts we will divide the interpretations on the role of protein components mediating the connections with the integrin (inside-out binding), in such a way that biochemical mechanisms are configured to promote affinity alterations for specific ligands. Generally, these mediations will occur by binding to actin filaments through talin (adaptor protein) or intermediate filaments<sup>37</sup>.

Thus, starting from the osteoblast cell membrane integrins, the only possibilities for binding of these proteins end up in:

The integrins  $\alpha_1\beta_2$ ,  $\alpha_2\beta_1$  are collagen receptors; the  $\alpha_2\beta_1$ ,  $\alpha_3\beta_1$ ,  $\alpha_5\beta_1$ ,  $\alpha_6\beta_1$ ,  $\alpha_v\beta_1$  are receptors for fibronectin; the  $\alpha_5\beta_1$  fibrinogen receptor; the  $\alpha_2\beta_1$  are receptors for laminin; the  $\alpha_3\beta_1$  is a receptor for epiligrin, thrombospondin and CSPG4.

Some  $\alpha_1$ ,  $\alpha_2$ ,  $\alpha_5$ ,  $\alpha_v$ ,  $\beta_1$ ,  $\beta_3$  subunits were not specified in the studies analysed. However, The  $\alpha_1$  subunit can only bind with  $\beta_1$  or  $\beta_2$ , and the  $\alpha_2$  can only bind with  $\beta_1$ , which in any case will characterize as collagen fiber receptor; the  $\alpha_5$  subunit can only and bind with  $\beta_1$ , which characterizes it as fibronectin receptor; the  $\beta_1$  subunit recognizes the RGD sequence on a wide range of ligands of  $\alpha_1$  (collagen fibers and laminin),  $\alpha_2$  (collagen fibers and laminin),  $\alpha_3$  (fibronectin, collagen fibers and laminin),  $\alpha_4$  (fibronectin and VCAM-1),  $\alpha_5$  (fibronectin),  $\alpha_6$  (laminin),  $\alpha_7$  (laminin),  $\alpha_8$  (osteopontin, vitronectin, fibronectin and nephronectin),  $\alpha_9$  (tenascin-C, VEGF-C and VEGF-D),  $\alpha_{10}$  (collagen fibers),  $\alpha_{11}$  (collagen fibers) and  $\alpha_v$  (fibronectin, vitronectin and osteopontin); the  $\beta_3$  subunit can only and make bonds with  $\alpha_{IIb}$  (fibronectin, fibrinogen, von Willebrand Factor, thrombospondin, and vitronectin) or with  $\alpha_v$  (osteopontin and collagenous fibers).

Thus, in the extracellular space the binding possibilities will be mediated with plasma proteins, complement system globulins and with the factors while the angiogenesis process occurs (initial moment). The salivary proteins will not have direct contact of specific binding with the membrane proteins, they will only subsidize the acquired film formation. As for the constituents of the extracellular matrix, we can highlight some bone matrix proteins such as BMP-2, IBSP, SPARC, OPG, BGLAP, SPP1, COL-1 and GAG that will participate in bone formation and remodeling. Thus, the possible and main structures between plastic membrane and implant, based on integrin binding possibilities, are: laminin, fibronectin, vitronectin and collagen fibers.

Laminin is a plasma membrane protein that constitutes the basal membrane. It is a receptor for integrin collagen fibers type IV, heparan sulfate (GAG) has as their main function the organization of the extracellular matrix.

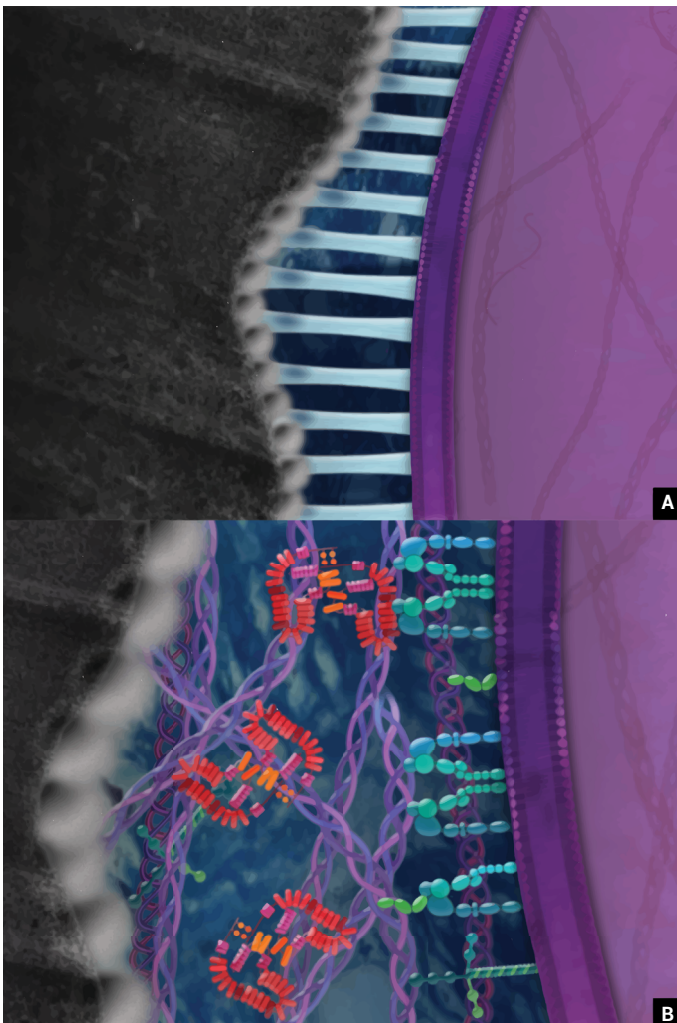
The fibronectin binds to cell surfaces by means of the integrin and is able to bind various compounds, including collagen fibers, fibrin, heparin, DNA and actin. It participates in the process of adhesion, cell locomotion, opsonization, regeneration, and maintenance of cell shape. It acts in the matrix assembly and thus in fibrillogenesis (essential for osteoblast mineralization), besides participating in the regulation of collagen fibers type I deposition (matrix secretion).

Vitronectin is an integrin receptor protein and can interact with GAG's and proteoglycans. It participates in cell adhesion and dissemination, literally functions as a cell-substrate adhesion molecule.

Collagen fibers type I (with portions of type III and V) are the main constituent of the extracellular matrix. They can bind with integrin, fibronectin, vitronectin. Specifically, collagen type IV (non-fibrillar) has an affinity for laminin, for collagens XV and XVIII, and proteoglycans.

Collagen fibers type VI associate with type I and III to form microfibrils and are stabilized by non-covalent GAG bonds; collagen fibers type XII also associate with collagen fibers type I; collagen type XV is a constituent of the basal membrane; collagen type XVII participates in the adhesion process of epithelial cells with the extracellular matrix and is a receptor for laminins and integrins.

Thus, our hypothesis is based on a structure similar to the basal membrane. When thinking about the concept in a broad way, the osteoconduction space will perform the role of basal membrane, since it has the same characterizations, the same constituents, and basically the same function. However, the concept of the basal membrane does not compete with the tissues involved, this being a characteristic, with high specificity of epithelial tissue (ectoderm), so that the basal membrane serves to join the epithelial tissue to the adjacent connective tissue. So, in this case, specifically, there is the bone tissue (mesoderm) and the implant, and both do not have any epithelial characteristic, because there is no epithelium, but there is specialized connective tissue (bone tissue). Therefore, it can be considered a structure similar and compatible with the basal membrane, but that is not characterized as the basal membrane, properly speaking. Thus, by convention we decided to call it the peri-implantar membrane, characterizing it as a delegate of the basal membrane, which has the delegated competence, but does not hold the position of basal membrane (Figure 4).



**Figure 4.** Interaction of Peri-implantar Membrane with the Implant Surface

Despite these perspectives, there is research exploring mechanisms of periodontal ligament regeneration in osseointegrable implants either through biomimetic routes, implant surface treatments, or even enzymatic routes. However, this study suggests that the ligament regenerates, or rather that there is an attempt to regenerate them.

Thus, due to virtually the same composition, it can be suggested that the periodontal ligament attempts to regenerate, however, due to some differences in specifications regarding constituents, and for not being able to provide the "nourishing function", there is a differentiation between both. Thus, we can consider that the peri-implant ligament can biomimicry the functions and composition of the periodontal ligament or consider that the peri-implant ligament is a consequence of the regeneration of the periodontal ligament.

In addition, the osseointegration concept has its complexity, especially in post-Brånemark concepts. Thus, understanding the role of these proteins during the osseointegration process is not something easy and simple. However, it is possible to distinguish that the proteins that participate in osteoblast adhesion are those that are part of the cell membrane and the proteins of the temporary matrix that are formed immediately after implant insertion.

Furthermore, it is suggestive that a ligamentous structure similar to the periodontal ligament is formed, since there is similarity in composition and function between both ligaments. After all, if there were no ligament between the implant and bone, there would be no distribution of masticatory loads and therefore maxillary/mandibular fracture would occur. Thus, the peri-implant ligament is a consequence of the osseointegration process.

In that manner, as a limitation of this study we can mention the absence of protein distinction in implants with different surface treatments because most of the results did not make this very clear. This limited a possible statistic about it.

However, the role of surface topography in implants is already known. There is already an identification of roughness and wettability parameters as well as surface treatments that directly influence the osseointegration process itself.

Furthermore, this study only considered the osseointegration process in the setting of systemic health and periodontal health. It disregards patients with different systemic health and periodontal conditions.

In conclusion, this systematic scoping review points to evidence suggesting the existence of a peri-implant ligament. This ligament has a composition similar to the periodontal ligament and can mimic sensory and support functions. However, future studies on molecular analysis regarding the composition of the peri-implant ligament and characterizations of this ligament are needed for a better understanding. This is in addition to longevity analyses regarding the success of osseointegrable implants, differences in ligament composition in relation to implant composition, and differences and changes in different periodontal profiles. Furthermore, the variants that can modulate the osseointegration process will probably also intervene in the formation process of this peri-implant membrane.

## Funding

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## Conflicts of interest

There is no conflict of interest in this project.

## Data availability statement

Datasets related to this article can be found at <https://osf.io/9sd5h/>, hosted at Open Science Framework (OSF).

## Author Contribution

**Nascimento, Souza, and Posch** reviewed the literature, developed the topics, and worked on the manuscript as well as the figures. All authors reviewed and approved the final version of the manuscript.

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