



# Immunomodulatory Role of Microelements in COVID-19 Outcome: a Relationship with Nutritional Status

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## Abstract

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease 2019 (COVID-19). SARS-CoV-2 infection can activate innate and adaptive immune responses and result in massive inflammatory responses in the disease. A comprehensive understanding of the participation of micronutrients in the immune response to COVID-19 will allow the creation of prevention and supplementation scenarios in malnutrition states. Microelement deficiency can be decisive in the progression of diseases and their optimal levels can act as protective factors, helping to maintain homeostasis. Vitamin A, B, D, selenium, zinc, and copper, through their complementary and synergistic effects, allow the components of innate and adaptive immunity to counteract infections like those occurring in the respiratory tract.

Thus, alterations in nutritional status are related to metabolic diseases, systemic inflammation, and deterioration of the immune system that alter the response against viral infections, such as COVID-19. The aim of this review is to describe the micronutrients that play an important role as immunomodulators and its relationship between malnutrition and the development of respiratory infections with an emphasis on severe and critical COVID-19. We conclude that although an unbalanced diet is not the only risk factor that predisposes to COVID-19, a correct and balanced diet, which provides the optimal amount of micronutrients and favors an adequate nutritional status, could confer beneficial effects for prevention and improvement of clinical results. The potential usefulness of micronutrient supplementation in special cases is highlighted.

**Keywords** SARS-CoV-2 · COVID-19 · Nutritional status · Micronutrients · Immune system · Microelements

## Introduction

SARS-CoV-2 has been spreading at high speed globally and with it, the emergence of the COVID-19 pandemic since December 2019. As of May 6, 2022, the World Health Organization (WHO) reported 513,955,910 confirmed cases of COVID-19 and more than 6.2 million deaths worldwide [1]. The lack of pharmacological treatments against COVID-19 urges us to highlight the importance of micronutrient-rich diets with a preventive approach. Immune system dysfunction due a poor diet and nutrient deficiency is a major risk

factor for respiratory virus infections that increase the burden of disease [2]. An optimal nutritional status is achieved through the consumption of a balanced and quality diet, which would provide all of the needed micronutrients in the appropriate quantity to guarantee an optimal response and thus prevent infections. Many studies suggest that nutrients are involved in the development of COVID-19 [2–5]; however, only a few of them directly assess nutrient deficiencies in patients with the disease, and fewer clinical assays study the influence of micronutrients in viral immune response.


There are several kinds of malnutrition: undernutrition, inadequate vitamins or minerals, overweight, obesity, and resulting diet-related non-communicable diseases [6]. Although the prevalence of malnutrition has decreased in recent decades, WHO [1] reported that 1.9 billion adults are overweight or obese, while 462 million are underweight. Obesity has increased uncontrollably and it coexists with underweight even in the same region of the world. The concept of the obesity-related double burden of malnutrition has

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# Antagonistic, synergistic, and additive antibacterial interaction between ciprofloxacin and amoxicillin against *Staphylococcus aureus*

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## Abstract

The aim of this in vitro study was to evaluate the interaction between ciprofloxacin and amoxicillin against beta-lactamase-producing *Staphylococcus aureus*. Concentration-dependent curves for each individual drug were carried out to obtain the mean inhibitory concentration in the agar well diffusion assay. Then, different ratios of the ciprofloxacin–amoxicillin combination (0.5:0.5, 0.8:0.2, 0.2:0.8, 0.9:0.1, 0.1:0.9, 0.95:0.05, and 0.05:0.95) were assessed. Data were analyzed using the isobolographic analysis and interaction index. The isobolographic evaluation shows that the 0.9:0.1 and 0.95:0.05 ratios of the ciprofloxacin–amoxicillin combination produced a synergistic antimicrobial interaction, the 0.8:0.2, 0.2:0.8, 0.1:0.9, and 0.05:0.95 proportions showed an additive antibacterial effect, and the 0.5:0.5 proportion induced antagonistic antimicrobial effects. The interaction index showed similar outcomes to the isobolographic analysis. In conclusion, the data of this study mainly show antimicrobial additive results of the ciprofloxacin–amoxicillin combination against beta-lactamase-producing *S. aureus*.

## KEYWORDS

amoxicillin, antimicrobial interaction, ciprofloxacin, *Staphylococcus aureus*

**Abbreviations:** *S. aureus*, *Staphylococcus aureus*; USA, United States of America; WHO, World Health Organization; DNA, Deoxyribonucleic acid; Cat., Catalogue; ATCC, American Type Culture Collection; MIC, Mean inhibitory concentration.

Eduardo Gómez-Sánchez and Mario Alberto Isiordia-Espinoza contributed equally, and both could be considered the first authors.

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## Centric relation- Maximum intercuspation Discrepancy. Bibliographic review.

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**ABSTRACT:** Centric relation is the starting point from which any treatment must be started, if this position is not stable, sliding from centric relation to maximum intercuspation will occur, this displacement is known as centric slide. The aim of the bibliographic review is to describe the origin and importance of centric slide in Dentistry. A bibliographic search was made for articles in Spanish and English; for selection, at least 15 articles published in the last 5 years were searched. During closure in centric relation position, the presence of cusp interference or premature contacts generates repositioning of the mandibular condyles. When centric slide is not properly evaluated, diagnosis and consequently the treatment plan can be incorrect. A discrepancy greater than 2.0 mm will require treatment. An ideal method for the measurement of the condylar position currently used is known as the condylar position indicator. The centric slide is present in 90% of cases, which indicates that centric relation and maximum intercuspation are not in the same position, besides they should not be confused. The use of an occlusal splint is recommended to correct centric slide.

**KEYWORDS:** Occlusion, Centric relation, Maximum Intercuspation, Centric Slide, Neuromuscular deprogramming.

### I. INTRODUCTION

Occlusion is defined as the connection of contact between dental arches, resulting from closure of the maxilla and the jaw by contraction of different muscles. The contacts that occur during occlusion can be static when the teeth contact at maximum intercuspation, or dynamic, when the teeth slide together with the jaw movement to achieve closure.<sup>1,2</sup>

Dentistry focuses on the functional evaluation of static and dynamic occlusion, as well as the temporomandibular joint and muscles. Its

importance lies in success or failure of treatments. Establishing an ideal occlusion is the basis and a requirement for successful diagnosis and therefore a good treatment plan.<sup>2</sup>

In order to establish an ideal occlusion we must know the meaning of centric relation and maximum intercuspation.

Maldonado et al.<sup>3</sup> establishes that the glossary of prosthodontic terms, defines centric relation (RC) as “the maxillamandibular relationship in which the condyles articulate with the thinnest and avascular portion of the articular disks with the complex in the most anterior and superior position against the walls of the articular eminence. This position is independent of dental contact.” It is considered a stable and reproducible physiological maxillary-mandibular relationship.<sup>4</sup>

Maximum intercuspation (MIC) is defined as the occlusal relationship in complete intercuspation of the teeth regardless of the position of the condyles.<sup>3</sup>

Centric relation is the starting point from which any treatment should be started, if this position is not stable, a sliding from centric relation to maximum intercuspation will occur, this displacement is known as centric slide.<sup>5</sup>

Several articles state that centric slide occurs in approximately 90% of people, some authors consider distraction from 1 to 2mm normal, while others consider it a problem that needs treatment from 2mm of distraction.<sup>6,7</sup>

The objectives of this bibliographic review are:

1. Emphasize the origin and importance of centric slide in Dentistry.
2. Specify the methods for recording the degree of condylar distraction.
3. Examine the relationship between centric slide and the presence of temporomandibular disorders.
4. Identify the treatment for correcting centric slide.



## Importance of the evaluation of the upper airways in dental practice

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**ABSTRACT:** The upper airways are part of the respiratory system. Their primary function is heating, humidifying and filtering the air. Anatomical and functional alterations in the upper airways can affect normal breathing, causing patients to mouth breathe.

Oral breathing can cause developmental craniofacial alterations, lip incompetence, small and underdeveloped nostrils, small upper lip, and oral cavity alterations like halitosis, cavities, periodontal disease and malocclusions.

A bibliographic search was made on different platforms like PUBMED, SciELO, among others, to obtain articles presenting upper airway alterations.

This bibliographic review enlists the most common upper airway alterations, to provide a guide for dentists on how to detect and refer them, and eliminate the cause of oral breathing.

**KEYWORDS:** upper airways, oral breathing, mouth breathing, nasal obstruction.

### I. INTRODUCTION

Normal breathing can be affected by anatomical and functional factors, causing the breathing process to be initiated on the mouth, instead of the nasal cavity.

Studies show that children with oral breathing are more likely to have trouble sleeping, and it is related to the presence of disorders such as Obstructive Sleep Apnea (OSA). Poor sleep quality causes fatigue during the day, irritability and even headaches. Some other studies even showed a relationship between oral respiratory disorders with a tendency of psychological disturbances, cognitive and emotional disorders. All of these symptoms can negatively affect the person's quality of life.<sup>1,2</sup>

Over the years the possible relation between upper airway morphology and craniofacial development has been studied for a correct diagnosis and orthodontic treatment,<sup>3</sup> due to their

correlation with the prevalence of certain oral conditions.

Airway morphology can cause alterations in respiratory function, resulting in facial and occlusal changes,<sup>4</sup> which can be presented in a modification of the dentoskeletal growth pattern or even focal problems like gingivitis due to oral breathing.

The aim of this study is to present different upper airway conditions that can cause oral breathing, to be able to identify them, be conscious of their treatment and the effects of these on patients, in order to raise awareness among the clinicians about the importance of their assessment in the dental practice.

### II. MATERIAL AND METHOD

A bibliographic review was made from articles taken from different sources such as: PUBMED, Science Direct, SciELO, Google Scholar and the database of the Autonomous University of Baja California; trying to obtain most of the literature no more than 5 years old. The review included articles written in Spanish and English languages. The key words were: upper airways, oral breathing, mouth breathing, nasal obstruction

### III. DEVELOPMENT

The upper airways are the part of the air-conduction system that encompasses the nasal cavity, nasopharynx, oropharynx, larynx, and the extrathoracic part of the trachea. Their structure and function directly affect the air conduction to the lower respiratory airways.<sup>3</sup>

These are of high importance, due to their participation in different systems. The particular functions of the upper airways are, heating, humidifying and filtering the air, also as an olfactory pathway, primary defense against infections, passage of the alimentary bolus and phonation.<sup>4,5</sup>



## Distraction osteogenesis in the treatment of temporomandibular dysfunctions

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### ABSTRACT: Introduction:

Distraction osteogenesis is a surgical technique in which two bone segments are gradually separated at the level of the condyle to promote and favor the formation of reparative and regenerative bone and cartilage tissue.

### Approach and justification:

Temporomandibular disorders constitute one of the main causes of attention in the clinical practice of dentistry. Understanding this type of disorders allows the clinician to identify the appropriate phase in which the dysfunction should be treated.

**Objective:** To evaluate the technique of distraction osteogenesis associated with TMJ ankylosis as a corrective interventional therapy and potential regenerative approach. **Methodology:** A search was performed in the database (Pubmed) considering the keywords: distraction osteogenesis, neocondyle regeneration, regenerative therapy, osteotomy, condylar regeneration, distraction device; articles were selected with a 6-year restriction. Results: In the craniofacial team setting the orthodontist assists in planning distraction surgery, developing or adapting distraction devices and in managing post-surgical outcomes.

**Conclusion:** The distraction osteogenesis technique represents a multidisciplinary alternative for the treatment of temporomandibular disorders associated with the integration of new diagnostic and planning technologies; although this alternative has certain advantages over other techniques, it presents certain limitations that can be eradicated by including regenerative therapy to the therapeutics associated with this clinical intervention.

**KEYWORDS:** Distraction osteogenesis, neocondyle regeneration, regenerative therapy, osteotomy, condylar regeneration, distraction device.

## I. INTRODUCTION

Osteogenic distraction is a process in which new bone formation occurs between two segments that are gradually separated by incremental traction.<sup>1,2</sup> Thanks to this it is possible to guide the bone formation taking into account the orientation in space to form a structural part of bone that is distracted. This technique was first used by Codivilla for femur lengthening, then McCarthy, et al. applied it to the craniofacial skeleton of children with congenital craniofacial anomalies.<sup>3</sup>

Temporomandibular disorders (TMD) constitute a complex and heterogeneous group of clinical conditions and alterations that affect the temporomandibular joints (TMJ), masticatory musculature, teeth and supporting apparatus, and therefore represent an important challenge for specialists in stomatology, because they represent an area of health with wide controversies in etiology, diagnosis and treatment.<sup>4</sup>

In general, TMD affect more than 50% of the world's population. Prevalence studies have shown that they are relatively frequent in the general population and it is estimated that 65% present at least one sign and 35% present at least one symptom, a product of the combination of malocclusion, emotional tension, stress and anxiety, among other psychogenetic factors, depending on the physiological tolerance or adaptive capacity of the individual.<sup>5,6</sup>

## II. METHODS

The aim of this study was to evaluate the technique of distraction osteogenesis associated with TMJ ankylosis as a corrective intervention therapy and the potential regenerative approach. To find this relationship, a database search was performed (Pubmed) considering the keywords: Distraction osteogenesis, neocondyle regeneration, regenerative therapy, osteotomy, cellular therapy,

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Jorge is full-time endodontics professor at the Autonomous University of Baja California, School of Dentistry, Tijuana campus.

**ENHANCED CPD**

GDC anticipated outcome: C

CPD hours: one

Topic: Endodontics

**Educational aims and objectives:**

To explore whether a controlled cleaning and shaping protocol reduces acute pain. This article qualifies for one hour of enhanced CPD; answer the questions on page 124 or scan the QR code.



**P**ost-endodontic discomfort is a common complication after root canal treatment (RCT). Acute pain can occur after an RCT procedure, particularly in necrotic teeth, and can turn to a flare-up (Morse, Koren and Esposito, 1986). The American Association of Endodontists (AAE) termed flare-up as a severe condition of an asymptomatic pulpal and/or radicular pathosis after the RCT.

This endodontic circumstance has a multifactorial origin; however, the extrusion of debris or other substance has been suggested as one of the main problems associated with post-endodontic pain.

Certain aetiological considerations play a part in post-endodontic pain, including: pre-endodontic pain; pulp condition; apical periodontitis; insufficient cleaning extrusion of organic materials; and filling outside the canal (Albashaireh and Alnegrish, 1998; Siqueira et al, 1997).

A successful RCT is achieved by meticulous and systematic preparation, disinfection and filling of the canals. Post-endodontic pain can be avoided if the clinician rigorously follows the steps of the selected technique to clean and shape the canals, manually or mechanically, which always results in some degree of debris extrusion (Siqueira et al, 1997; Kakehashi, Stanley and Fitzgerald, 1965).

Removal of bacteria from the canals is an

important step in RCT (Kakehashi, Stanley and Fitzgerald, 1965; Möller et al, 1981; Abbott and Yu, 2007). NaOCl is an irrigant that has an anti-biofilm capacity (Soares and César, 2001; Ricucci and Siqueira, 2010; Dutner and Mines, 2012; Willershausen et al, 2015).

Together with the interruption of biofilms, the reduction of microorganisms is accomplished by mechanical instrumentation and flushing using microbicide mixes in the canal between visits (Swimberghe et al, 2018; Busanello et al, 2019; Petridis et al, 2019).

While cleaning and shaping the canal, remains and irrigating solutions can be sent beyond the apex, leading to postoperative complications, such as intense pain or flare-ups. Therefore, adequate care of the working length (WL) can diminish the expulsion of remains through the apical foramen.

Engine-driven instruments can be either rotary or reciprocating to clean and shape the canals. Many studies consider the kinematics of root canal preparation to avoid post-endodontic pain. Single-visit RCT is established on the clinical judgment that additional treatments would not increase the superiority of care (Glennon et al, 2004). Microbial elimination cannot probably be increased without calcium hydroxide dressing between visits (Peters and Wesselink, 2002).

Tooth group	One-visit treatment (n = 45) (%)	One-visit treatment (n = 45) (%)	Two-visit treatment (n = 45) (%)	Two-visit treatment (n = 45) (%)
Group 1a	15 (33.33%)	14 (31.11%)		
Group 1b			15 (33.33%)	15 (33.33%)
Group 2a	15 (33.33%)	15 (33.33%)		
Group 2b			15 (33.33%)	14 (31.11%)
Control group 3a	15 (33.33%)	15 (33.33%)		
Control group 3b			15 (33.33%)	14 (31.11%)

**TABLE 1:** Distribution of teeth by randomisation factors

**Jorge Paredes Vieyra** explores whether a controlled cleaning and shaping protocol would result in a reduced acute pain rate of single versus two-visit RCT of teeth with necrotic pulp and apical periodontitis

# Acute pain reduction: clinical trial

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# A Comparative Overview of Working Length Determination with Radiographs and Two Electronic Apex Locators

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and **Amairani Denisse Sánchez González**<sup>a#</sup>

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## ABSTRACT

**Aim:** To evaluate the accuracy of the Root ZX and Elements-Diagnostic electronic apex locators when compared to radiographs for locating the canal terminus or minor foramen.

**Methodology:** The canal terminus of 482 canals in 160 maxillary and mandibular teeth was located in vivo with both locators and radiographically. After extraction the actual location of the minor foramen was determined visually and with magnification. A paired samples t test, X2 test and a repeated measure ANOVA at the 0.05 level of significance were used to determine differences between the groups.

**Results:** The Root ZX located the minor foramen correctly 68% of the time in anterior and premolar teeth, and 58% of the time in molar teeth. The Elements-Diagnostic located the minor foramen correctly 58% of the time in anterior and premolar teeth and 49% of the time in molar teeth. Radiographs located the minor foramen correctly 20% of the time in anterior and premolar teeth and 11% of the time in molar teeth. There was no statistically significant difference between the two locators but there was a significant difference between them and radiographs. For all teeth, the measurements made by the apex locators were within  $\pm 0.5$  mm of the minor foramen 100% of the time, whereas for the radiographs, the measurements were within this range only 15% of the time. This difference was significant ( $p=0.05$ ).

**Conclusion:** Measuring the location of the minor foramen using the two apex locators was more accurate than radiographs and would reduce the risk of instrumenting and filling beyond the apical foramen.

**Keywords:** *Electronic apex locator; root ZX; elements-diagnostic; working length determination; apical constriction.*

## 1. INTRODUCTION

Root canal preparation and filling should not extend beyond the tooth root nor leave uninstrumented areas inside the root canal. Anatomically, the apical constriction (AC), also called the minor apical diameter or minor diameter [1], is a logical location for working length (WL) since it often coincides with the narrowest diameter of the root canal (AAE 2003). However, locating the AC clinically is problematic. Dummer et al. (1984) concluded that it is impossible to locate the minor foramen clinically with certainty because of its position and topography. The cementodentinal junction (CDJ) has also been suggested as the location for WL because it represents the transition between pulpal and periodontal tissue [2]. The location of the CDJ is widely accepted as being 0.50 mm to 0.75 mm coronal to the apical foramen [3] but, as with the AC, the exact location of the CDJ is impossible to

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## Translational dentistry: stem cell and tissue engineering in regenerative dentistry

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**ABSTRACT:**Currently there is great interest in the therapeutic application of stem cells for tissue regeneration, this being a topic of global scientific interest. Current reports on mesenchymal stem cells indicate that it is possible to isolate several cells from different adult tissues, including bone marrow, neural tissue, muscle, skin, retina, cornea, among others. Regarding the use of mesenchymal stem cells from the oral cavity, it is reported that, from them, both those that have their origin in the dental pulp and those present in the periodontal ligament, in the apical papilla, the dental sac and other regions mucous membranes of the oral cavity, the formation of structures belonging to the dentin-pulp and periodontal complexes is possible. Likewise, their ability to stimulate new bone formation is reported, so they have a possible application in craniofacial bone regeneration.

One of the main advantages offered by the isolation of mesenchymal stem cells from the oral cavity over other means of obtaining, is the accessibility and easy handling of the samples, as well as the minimally invasive and painless techniques, compared to those obtained from bone marrow.

Due to their multipotential nature, families of mesenchymal stem cells from the oral cavity are a rich source of cell complexes that, by means of specific activation and induction techniques, have the capacity to differentiate into other cell complexes, which at a given moment can be used in therapies of regeneration associated with tissue engineering and regenerative medicine.

**KEYWORDS:**Mesenchymal stem cells, tissue engineering, regenerative medicine, bone defects, translational dentistry.

### I. INTRODUCTION

A stem cell is a forming cell, undifferentiated, with the ability to self-renew (that is, produce other cells in a tissue), through cell

division; being able to carry out a specific cell differentiation by following an autonomous or induced differentiation pathway or guide, and, therefore, being able to form cells of one or more tissues; mature, functional, specific, and differentiated.

[1] It is possible to classify this cell group into two main ranges:

#### A. According to the origin or means of obtaining:

**Embryonic stem cells(ESC:** Embryonic Stem Cells).They derive from the inner cell mass of the embryo at the blastocyst stage (7-14 days of embryonic development). They can generate the three embryonic tissues: endoderm, mesoderm, and ectoderm.

**Specific adult stem cells or organ.**They derive from the mitotic division of embryonic stem cells, found in adult organs or tissues, and can generate specific cells for a tissue or organ. In this cell group, we can find the stem cells of the umbilical cord, the hematopoietic stem cells, and the undifferentiated mesenchymal stem cells, where those that have an origin from a tissue or structure of the dental cavity or oral cavity stand out.

#### B. According to its ability to differentiate:

**Totipotent stem cells.**They are those cells with the ability to grow and form a complete organism, both in embryonic and extra-embryonic components.

**Pluripotent stem cells.**To this group belong all those cells capable of producing cell groups corresponding to tissues in embryonic development and in mature structures.

**Multipotential cell groups.**They are those capable of only differentiating into a limited number of cells. An example is the bone marrow, which can differentiate into blood cells (red blood cells, white blood cells and platelets).

**Unipotently cell groups.**Cells with the ability to form only one cell type belong to this group.



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## **Cultivo, aislamiento e identificación de células madre de pulpa dental: una alternativa en medicina regenerativa.**

Culture, isolation, and identification of dental pulp stem cells: a regenerative medicine alternative.

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### **PALABRAS CLAVE**

andamio, células madre, constructo tisular, inmunohistoquímica, linaje osteogénico, medicina regenerativa.

### **KEYWORDS**

scaffold, stem cell, tissular construct, immunohistochemical, osteogenic lineage, regenerative medicine.

### **RESUMEN**

En la actualidad la medicina regenerativa e ingeniería de tejidos establecen una sinergia de interés científico global. La aplicación terapéutica de células madre de pulpa dental debido a su capacidad de proliferación e inducción, demuestran su alto potencial regenerativo. Los defectos óseos derivados de lesiones traumáticas o enfermedades degenerativas comprometen las expectativas de recuperación debido a los tratamientos radicales y a los pobres resultados que éstos ofrecen. Por tal motivo, éste estudio tiene como propósito fundamental el cultivo exitoso de células madre y su validación histoquímica, con una visión futura en su caracterización e inducción al linaje osteogénico para su implementación en un constructor tisular, formado por las células madre, un biopolímero y un agente inductor necesarios para la configuración de un sistema tisular. En conclusión, los resultados muestran que a partir de la pulpa dental es posible aislar células madre capaces de proliferar, ser identificadas por inmunohistoquímica con un alto potencial de organización creando un microambiente celular óptimo que asegura la regeneración tisular exitosa, en un menor periodo de tiempo, con mejores resultados y expectativas de recuperación.

### **ABSTRACT**

Currently regenerative medicine and tissue engineering establish a synergy of global scientific interest. Therapeutic application of dental pulp stem cells due to their proliferation and induction capabilities demonstrates their high regenerative potential. Bone defects arising from traumatic injuries or degenerative diseases compromise recovery expectations due to radical treatments and the poor results they offer. For this reason, the fundamental purpose of this study is the successful cultivation of stem cells of dental pulp and its immunohistochemical validation, with a future vision in its characterization and cellular induction to the osteogenic lineage, for its implementation in a tissue construct: formed by stem cells, a biopolymer and an inducing agent for cell implantation and proliferation, necessary in the configuration of the tissue system. In conclusion, the results show that from dental pulp it is possible to isolate stem cells capable of proliferating, be identified by immunohistochemistry with a high potential for differentiation and organization in a scaffold can be implanted in an area of bone injury, thus it is possible to produce successful tissue regeneration, in a shorter period, with better results and recovery expectations.

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## **El citoesqueleto de actina: su importancia en la formación y mantenimiento de los microambientes tisulares.**

The actin cytoskeleton: its importance in the formation and maintenance of tissue microenvironments.

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### **PALABRAS CLAVE**

andamio, células mesenquimales, citoesqueleto, ingeniería de tejidos, inmunomarcaje.

### **KEYWORDS**

scaffold, mesenchymal cells, cytoskeleton, tissue engineering, immunostaining.

### **RESUMEN**

Los microfilamentos de actina del citoesqueleto presentes en las células de cultivos obtenidos in vitro les otorgan a estas un dinamismo adaptativo, presentes en el ambiente natural dentro de los tejidos. La célula en el cultivo debe adaptarse y relacionarse exitosamente mediante el correcto manejo de las muestras y la estandarización de las técnicas de identificación, aislamiento y validación. Para el desarrollo de esta investigación se realizaron cultivos celulares primarios y secundarios a partir de pulpa dental mediante la técnica de explantes tisulares, cultivados y monitoreados bajo condiciones controladas, enriquecidos y suplementados con medio de cultivo estandarizado y selectivo. Los ensayos de validación estructural y funcional corresponden a la técnica de inmunomarcaje triple por microscopia confocal giratoria, tanto para la identificación de células mesenquimales como de estructuras intra y extracelulares. Como resultado se obtuvieron células mesenquimales activas en su fase de mitosis con una dinámica de relación y comunicación celular adecuada, expresando actividad nuclear y de componentes del citoesqueleto de actina unidireccionales (fibras de estrés, córtex y microespiculas) y multidireccionales (filopodios y lamelipodios) con lo que se confirma el desarrollo de un microambiente celular óptimo y se propone el uso de estos complejos celulares para el desarrollo de constructos tisulares evaluados en biomodelos como terapia regenerativa en ingeniería de tejidos.

### **ABSTRACT**

The actin microfilaments of the cytoskeleton present in cultured cells obtained in vitro give these cells an adaptive dynamism, present in the natural environment within tissues. The cell in culture must adapt and relate successfully through the correct handling of samples and the standardization of identification, isolation, and validation techniques. For the development of this research, primary and secondary cell cultures were performed from dental pulp using the tissue explant technique, cultured and monitored under controlled conditions, enriched and supplemented with standardized and selective culture medium. Structural and functional validation assays correspond to the triple immunolabeling technique by spinning confocal microscopy, both for the identification of mesenchymal cells and intra- and extracellular structures. As a result, active mesenchymal cells were obtained in their mitosis phase with an adequate relationship dynamics and cell communication, expressing nuclear activity and unidirectional (stress fibers, cortex and microspicules) and multidirectional (filopodia and lamellipodia) actin cytoskeleton components, thus confirming the development of an optimal cellular microenvironment and proposing the use of these cell complexes for the development of tissue constructs evaluated in biomodels as regenerative therapy in tissue engineering.

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## **Desarrollo de un constructo tisular por técnica de descelularización traqueal.**

Development of a tissue construct by tracheal decellularization technique

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### **PALABRAS CLAVE**

constructo, descelularización, citoesqueleto, ingeniería de tejidos, inmunofluorescencia, recelularización.

### **KEYWORDS**

construct, decellularization, cytoskeleton, tissue engineering, immunofluorescence, recellularization.

### **RESUMEN**

La ingeniería de tejidos es un área científica interdisciplinaria que tiene como fundamento principal, la creación e implantación de sustitutos biológicos con el objetivo de reparar, reemplazar, mantener o mejorar la función específica de un tejido u órgano. Mediante la combinación de aspectos tecnológicos novedosos e innovadores, la ingeniería de tejidos y de órganos tiene una nueva herramienta de reemplazo celular, por medio del uso de células troncales o madre las cuales pueden ser cultivadas, aisladas y diferenciadas en el laboratorio para su posterior incorporación a un órgano o tejido dañado induciendo directamente su reparación estructural y funcional. El cuerpo humano, es un sistema biológico activo interactivo, en el cual, se desarrollan simultánea y sistemáticamente funciones vitales de supervivencia, mediante la interacción de complejos celulares, tejidos y órganos, los cuales conjuntan sus funciones individuales y grupales específicas para el mantenimiento de su integridad. La pérdida funcional o estructural de forma parcial o total de un tejido u órgano, es una condición que afecta frecuentemente y representa un grave problema de salud pública por su incidencia y costos. Debido a esta creciente necesidad de órganos, se han establecido investigaciones recientes sobre el uso de células autólogas<sup>1</sup> para la reconstrucción de tejidos y órganos, asegurando la biocompatibilidad<sup>2</sup> y evitando así las terapias inmunosupresoras las cuales no aseguran la aceptación del tejido u órgano trasplantado, con lo cual se abre un nuevo campo en la medicina regenerativa, la regeneración tisular y regeneración orgánica directa.

### **ABSTRACT**

Tissue engineering is an interdisciplinary scientific area whose main foundation is the creation and implantation of biological substitutes with the aim of repairing, replacing, maintaining, or improving the specific function of a tissue or organ. Through the combination of new and innovative technological aspects, tissue and organ engineering has a new cell replacement tool, using stem or stem cells which can be cultivated, isolated, and differentiated in the laboratory for their subsequent incorporation into a damaged organ or tissue directly inducing its structural and functional repair. The human body is an interactive active biological system, in which vital functions of survival are developed simultaneously and systematically, through the interaction of cellular complexes, tissues and organs, which combine their specific individual and group functions for the maintenance of their health. integrity. The partial or total functional or structural loss of a tissue or organ is a condition that frequently affects and represents a serious public health problem due to its incidence and costs. Due to this growing need for organs, recent research has been established on the use of autologous cells for the reconstruction of tissues and organs, ensuring biocompatibility and thus avoiding immunosuppressive therapies which do not ensure acceptance of the transplanted tissue or organ, thus which opens a new field in regenerative medicine, tissue regeneration and direct organic regeneration.

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## Distraction osteogenesis in the treatment of temporomandibular dysfunctions

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### ABSTRACT: Introduction:

Distraction osteogenesis is a surgical technique in which two bone segments are gradually separated at the level of the condyle to promote and favor the formation of reparative and regenerative bone and cartilage tissue.

### Approach and justification:

Temporomandibular disorders constitute one of the main causes of attention in the clinical practice of dentistry. Understanding this type of disorders allows the clinician to identify the appropriate phase in which the dysfunction should be treated.

**Objective:** To evaluate the technique of distraction osteogenesis associated with TMJ ankylosis as a corrective interventional therapy and potential regenerative approach. **Methodology:** A search was performed in the database (Pubmed) considering the keywords: distraction osteogenesis, neocondyle regeneration, regenerative therapy, osteotomy, condylar regeneration, distraction device; articles were selected with a 6-year restriction. Results: In the craniofacial team setting the orthodontist assists in planning distraction surgery, developing or adapting distraction devices and in managing post-surgical outcomes.

**Conclusion:** The distraction osteogenesis technique represents a multidisciplinary alternative for the treatment of temporomandibular disorders associated with the integration of new diagnostic and planning technologies; although this alternative has certain advantages over other techniques, it presents certain limitations that can be eradicated by including regenerative therapy to the therapeutics associated with this clinical intervention.

**KEYWORDS:** Distraction osteogenesis, neocondyle regeneration, regenerative therapy, osteotomy, condylar regeneration, distraction device.

## I. INTRODUCTION

Osteogenic distraction is a process in which new bone formation occurs between two segments that are gradually separated by incremental traction.<sup>1,2</sup> Thanks to this it is possible to guide the bone formation taking into account the orientation in space to form a structural part of bone that is distracted. This technique was first used by Codivilla for femur lengthening, then McCarthy, et al. applied it to the craniofacial skeleton of children with congenital craniofacial anomalies.<sup>3</sup>

Temporomandibular disorders (TMD) constitute a complex and heterogeneous group of clinical conditions and alterations that affect the temporomandibular joints (TMJ), masticatory musculature, teeth and supporting apparatus, and therefore represent an important challenge for specialists in stomatology, because they represent an area of health with wide controversies in etiology, diagnosis and treatment.<sup>4</sup>

In general, TMD affect more than 50% of the world's population. Prevalence studies have shown that they are relatively frequent in the general population and it is estimated that 65% present at least one sign and 35% present at least one symptom, a product of the combination of malocclusion, emotional tension, stress and anxiety, among other psychogenetic factors, depending on the physiological tolerance or adaptive capacity of the individual.<sup>5,6</sup>

## II. METHODS

The aim of this study was to evaluate the technique of distraction osteogenesis associated with TMJ ankylosis as a corrective intervention therapy and the potential regenerative approach. To find this relationship, a database search was performed (Pubmed) considering the keywords: Distraction osteogenesis, neocondyle regeneration, regenerative therapy, osteotomy, cellular therapy,



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## **Odontología traslacional: ingeniería de tejidos en las ciencias clínicas odontológicas**

Culture, insolation, and identification of dental pulp stem cells: a regenerative medicine alternative.

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### **PALABRAS CLAVE**

andamio, células madre, constructo tisular, inmunohistoquímica, linaje osteogénico, medicina regenerativa.

### **KEYWORDS**

scaffold, stem cell, tissular construct, immunohistochemical, osteogenic lineage, regenerative medicine.

### **RESUMEN**

Recientemente se ha incorporado a la investigación clínica odontológica un campo de conocimiento altamente prometedor, la ingeniería de tejidos. Los principales objetivos de este novedoso campo están encaminados a la regeneración, reparación o reemplazo de tejidos, que han sido dañados por diversas implicaciones clínicas o anomalías congénitas. En lo que se refiere a la regeneración de tejidos como la pulpa, el hueso alveolar y la mucosa oral, se han realizado avances importantes que han trascendido a la atención clínica del paciente. La Ingeniería Tisular da lugar a un nuevo campo en la odontología: la odontología traslacional que suma los conceptos asociados a la ingeniería de tejidos y la medicina regenerativa ofreciendo al paciente alternativas de tratamiento enfocadas a la regeneración de tejidos, tal es el caso de la dentina que es un tejido de soporte estructural del diente, que si bien la caries dental puede afectarla, tiene la capacidad de repararse de manera limitada pero con capacidades de regeneración que pueden aprovecharse desde el punto de vista de la odontología traslacional.

### **ABSTRACT**

A highly promising field of knowledge, tissue engineering, has recently been incorporated into dental clinical research. The main objectives of this new field are aimed at the regeneration, repair, or replacement of tissues, which have been damaged by various clinical implications or congenital abnormalities. About the regeneration of tissues such as the pulp, alveolar bone and oral mucosa, important advances have been made that have transcended the clinical care of the patient. Tissue Engineering gives rise to a new field in dentistry: translational dentistry that adds the concepts associated with tissue engineering and regenerative medicine, offering the patient treatment alternatives focused on tissue regeneration, such is the case of dentin. which is a structural support tissue of the tooth, which although dental caries can affect it, has the capacity to repair itself in a limited way but with regeneration capacities that can be used from the point of view of translational dentistry.

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## **Aplicaciones de la impresión 3d en odontología**

3D printing applications in dentistry

### **Autores:**

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### **PALABRAS CLAVE**

impresión 3D, fabricación aditiva, bioimpresión, tomografía de haz cónico, odontología, ingeniería de tejidos, diseño asistido por computadora (CAD), fabricación asistida por computadora (CAM)

### **KEYWORDS**

3D printing, additive manufacturing, cone beam tomography, dentistry, tissue engineering, computer aided design (CAD), computer aided manufacturing (CAM).

### **RESUMEN**

La tecnología de impresión 3D o también llamada fabricación aditiva, tiene sus inicios desde 1983 y ha evolucionado hasta los diferentes sistemas de fabricación que existen en la actualidad, los cuales han tenido un auge importante en la odontología en la última década. Este trabajo presenta, a través de una revisión de la literatura, una visión general sobre la aplicación de la impresión 3D en las diferentes áreas de la odontología, los distintos métodos y sistemas que existen para ello e identifica las áreas de oportunidad para ampliar su aplicación. Se realizó una revisión de la literatura con información recolectada de PubMed, MedLine, Google académico, tomando 37 artículos que cumplieron con los criterios de selección. Se encontró que existen distintos métodos de fabricación asistida que pueden ser utilizados dentro de la odontología, siendo los materiales poliméricos los que ofrecen mayor versatilidad, seguidos de los metales y cerámicas. La bioimpresión por su parte permite la posibilidad de adicionar células y factores de crecimiento a las impresiones ofreciendo una importante alternativa para la regeneración tisular. La impresión 3D tiene un inmenso potencial para el mejoramiento de la educación, investigación y tratamientos odontológicos, pero es importante que se continúe trabajando en el desarrollo de nuevos biomateriales para impresión con mejores propiedades que permitan una mayor aplicación de la técnica.

### **ABSTRACT**

3D printing technology, also known as additive manufacturing, has its beginnings since 1983 and has evolved towards the different systems that exist today, which have had an important boom in dentistry over the last decade. The present work show through a literature review, an overview of 3D printing applications in different areas of dentistry, the different printing methods available and identification of areas of opportunity to expand its application. Literature review was made with information collected from PubMed, MedLine, Google scholar, taking 37 articles that met the selection criteria. The findings were that there are different additive manufacturing methods that can be used in dentistry, and polymeric materials are the most versatile, followed by metals and ceramics. Bioprinting allows the possibility to add

# **Endodoncia traslacional e ingeniería de tejidos**

Translational endodontics and tissue engineering

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## **PALABRAS CLAVE**

Endodoncia regenerativa, ingeniería de tejido, regeneración pulpar, células troncales, andamio.

## **KEYWORDS**

regenerative endodontics, tissue engineering, dental pulp regeneration, stem cells, scaffold.

## **RESUMEN**

En la actualidad es cada vez más conocida la aplicación terapéutica de células troncales para la regeneración de tejidos provocando un mayor interés a nivel mundial en el tema. La preservación del tejido pulpar con su vasculatura y sus componentes nerviosos sigue siendo hoy en día un desafío dentro de la odontología moderna; siguiendo los principios de la ingeniería de tejido, la combinación de células madre, andamio y factores de crecimiento es como se ha podido trasladar los esfuerzos de la investigación al área clínica, permitiendo así revolucionar la perspectiva del campo de la endodoncia. De acuerdo con la Asociación Americana de Endodoncia las fracturas verticales se originan en el ápice y se desplazan hacia la corona. Alguna literatura comenta que es la tercera razón por la que hay una extracción en dientes tratados endodónticamente a diferencia de los dientes que permanecen con vitalidad pulpar, es por ello que la posibilidad de ofrecer una alternativa de erradicación del problema de inflamación pulpar (pulpitis irreversible) o bacteriana (necrosis) realizando el correcto debridamiento del espacio del conducto radicular así como un adecuado protocolo de desinfección donde la alternativa a ofrecer se da en la posibilidad de sellar el conducto con células mesenquimales de pulpa colocadas sobre un andamio disminuyendo así el porcentaje de fracturas en dientes con tratamiento endodónticamente.

## **ABSTRACT**

At present, the therapeutic application of stem cells for tissue regeneration is increasingly known, causing greater interest worldwide in the subject. Preservation of the pulp tissue with its vasculature and nerve components continues to be a challenge in modern dentistry today; Following the principles of tissue engineering, the combination of stem cells, scaffold and growth factors is how it has been possible to transfer research efforts to the clinical area, thus allowing to revolutionize the perspective of the field of endodontics. According to the American Endodontic Association, vertical fractures originate at the apex and move towards the crown. Some literature comments that it is the third reason why there is an extraction in endodontically treated teeth as opposed to teeth that remain with pulp vitality, which is why the possibility of offering an alternative to eradicate the problem of pulp inflammation (irreversible pulpitis) or bacterial (necrosis) performing the correct debridement of the root canal space as well as an adequate disinfection protocol where the alternative to be offered is the possibility of sealing the canal with mesenchymal pulp cells placed on a scaffold, thus reducing the percentage of fractures in teeth with endodontic treatment

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# Immunomodulation by *Bifidobacterium animalis* subsp. *lactis* Bb12: Integrative Analysis of miRNA Expression and TLR2 Pathway–Related Target Proteins in Swine Monocytes

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## Abstract

*Bifidobacterium animalis* subsp. *lactis* Bb12 is a widely used probiotic that provides numerous health benefits to its host, many due to its immunomodulatory properties. Although the precise mechanism of modulation is still under investigation, several reports associate the interaction of TLR2 with components of the bacterial cell wall inducing a signaling cascade that culminates with the production of cytokines and co-stimulatory molecules. MicroRNAs (miRNAs) have emerged as important post-transcriptional regulators of immune responses, including those toward probiotics. In this study, we analyzed the miRNA expression profile in swine monocytes exposed to Bb12 by using an anti-TLR2 blocking strategy and Bb12 involvement in the regulation of the TLR2 pathway. As a result, the expression of 40 miRNAs was influenced by the treatments ( $p < 0.01$ ), and 15 differentially expressed miRNAs with validated miRNA–mRNA interactions with around 26 proteins related to the TLR2 pathway were identified. The miRNAs upregulated in response to Bb12 included miR-15a-5p, miR-16-5p, miR-26a-5p, miR-29b-3p, and miR-30d-5p, and the following showed downregulation: miR-181a-5p, miR-19b-3p, miR-21-5p, miR-23a-5p, and miR-221-3p. The expression of let-7c-5p, let-7f-5p, miR-146b-5p, miR-150-5p, and miR-155-5p was increased by Bb12 only when TLR2 was blocked. The identified miRNA common targets were downstream proteins from bacterial recognition via TLR2, such as MyD88, TRAF6, and MAPK members; transcription factors such as NF- $\kappa$ B and AP-1; and cytokines such as IL-6, IL-10, and TNF- $\alpha$ . TLR2 participation was abrogated by anti-TLR2 antibody and suggests that bacterial recognition is complemented by other receptors since there were still changes in the microtranscriptome.

**Keywords** *Bifidobacterium* · miRNAs · TLR2 · Swine · Probiotics

## Introduction

Probiotic microorganisms have been widely studied due to their beneficial effects on the health of vertebrates, including animals. *Bifidobacterium animalis* subsp. *lactis* Bb12 (Bb12), one of the most studied probiotic organisms, has been shown to improve intestinal function, to enhance protection against infectious diarrhea, and to reduce the secondary effects of antibiotic treatment [1]. Bb12 has also been shown to be immunomodulatory, inducing the production of interleukin (IL)-10 and moderately IL-12 in immune cells [2]. The main mechanism of immune stimulation by Gram-positive bacteria such as Bb12 is mediated by receptor recognition of bacterial cell membrane components, like peptidoglycans (PGNs) and lipoteichoic acid (LTA), for which eukaryotic cells have specific receptors including toll-like receptor 2 (TLR2). Upon binding,

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## Review

# MicroRNAs Encoded by Virus and Small RNAs Encoded by Bacteria Associated with Oncogenic Processes

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**Abstract:** Cancer is a deadly disease and, globally, represents the second leading cause of death in the world. Although it is a disease where several factors can help its development, virus induced infections have been associated with different types of neoplasms. However, in bacterial infections, their participation is not known for certain. Among the proposed approaches to oncogenesis risks in different infections are microRNAs (miRNAs). These are small molecules composed of RNA with a length of 22 nucleotides capable of regulating gene expression by directing protein complexes that suppress the untranslated region of mRNA. These miRNAs and other recently described, such as small RNAs (sRNAs), are deregulated in the development of cancer, becoming promising biomarkers. Thus, resulting in a study possibility, searching for new tools with diagnostic and therapeutic approaches to multiple oncological diseases, as miRNAs and sRNAs are main players of gene expression and host-infectious agent interaction. Moreover, sRNAs with limited complementarity are similar to eukaryotic miRNAs in their ability to modulate the activity and stability of multiple mRNAs. Here, we will describe the regulatory RNAs from viruses that have been associated with cancer and how sRNAs in bacteria can be related to this disease.

**Keywords:** microRNA; small RNAs; oncogenesis; viruses; bacteria

## 1. Introduction

In addition to RNAs that encode proteins, different types of genes produce RNAs that are not translated into proteins and are called noncoding RNAs (ncRNAs). All the functions of ncRNAs are still unknown. However, it has been shown that many of them can play essential functions in the regulation of transcription and translation. Moreover, they have even been identified as playing important roles in normal physiological processes and some human diseases [1,2].

NcRNAs have been divided according to their size. RNAs with a size of less than 200 nt are classified as small noncoding RNAs (sncRNA), these include small interfering RNAs (siRNA), miRNA, and RNA that interact with piwi (piRNA). NcRNAs with a size greater than 200 nt are classified as long noncoding RNA (lncRNA) [3].

## Synthesis of BODIPY-Amino Acids and the Potential Applications as Specific Dyes for the Cytoplasm of Langerhans $\beta$ -Cells

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In this work, we explored the synthesis of 4,4-difluoro-4-bora-3a,4a-diazas-indacene (BODIPYs) bound to five different amino acids (BODIPY-FAA) (glycine, alanine, leucine, phenylalanine, and tyrosine) (amino group is kept protected with fluorophore Fmoc) and evaluated these conjugates in terms of (i) their photophysical properties and (ii) their potential application as cell staining agents of suspension and adherent cells at healthy and stress conditions. In general, all synthesized BODIPY-FAA (**3a-3e**) were found to emit fluorescence in the blue and green regions of the spectrum (depending on the solvent conditions). However, BODIPY-FTyr(trt) (**3e**) showed the best molar extinction coefficient ( $\epsilon = 28,198 \text{ M}^{-1} \text{ cm}^{-1}$ ) and quantum yield ( $\Phi = 0.17$ ). Biologically speaking, all synthesized conjugates demonstrated a selective affinity for the cytoplasm of Langerhans  $\beta$ -cells employed as a model, being the BODIPY-FLeu conjugate the one displaying the highest observed intensity. As such, our results reveal the BODIPY-FAA as a novel attractive tool for the specific staining of the cell cytoplasm, demonstrating not only a dual fluorescence emission but also a sensing capability to recognize different cell states.

**Keywords:** BODIPY-amino acids dyes, bio-conjugation, cell staining

### Introduction

Amino acids are one of the most important blocks in biological processes.<sup>1</sup> Moreover, amino acids are natural inducers of structural specificity at the intracellular level since their interaction with cell surfaces produces different and selective results, likewise, amino acids are molecules that are recognized by the biological system and are biocompatible. Among others, they are involved in the

formation of peptides and proteins, and in the course of any aberrant alteration in protein folding at a physiological level often manifested in common metabolic disorders, serious neurological conditions such as Alzheimer and Parkinson diseases, as well as cardiovascular diseases,<sup>2,3</sup> Branched-chain,<sup>4</sup> aminoaciduria, glutaric acidurias, phenylketonuria, nonketotic hyperglycinemia, homocystinuria, etc. The ascertaining of the L-amino acids in a biological system is of great importance since they are an essential part of the metabolism of proteins and physiology. The amino acids found in the intestine, especially those with

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## Article

# Optimizing the Efficiency of a Cytocompatible Carbon-Dots-Based FRET Platform and Its Application as a Riboflavin Sensor in Beverages

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**Abstract:** In this work, the Förster resonance energy transfer (FRET) between carbon dots (CDs) as energy donors and riboflavin (RF) as an energy acceptor was optimized and the main parameters that characterize the FRET process were determined. The results were successfully applied in the development of an ultrasensitive ratiometric fluorescent sensor for the selective and sensitive determination of RF in different beverages. Water-soluble CDs with a high quantum yield (54%) were synthesized by a facile and direct microwave-assisted technique. The CDs were characterized by transmission electron microscopy (TEM), Fourier transform infrared spectroscopy (FTIR), dynamic light scattering (DLS), Zeta potential, and UV-visible and molecular fluorescence spectroscopy. The study of the FRET process at two donor concentrations showed that the energy transfer efficiency decreases as the donor concentration increases, confirming its dependence on the acceptor:donor ratio in nanoparticle-based systems. The results show the importance of optimizing the FRET process conditions to improve the corresponding output signal. The variation in the ratiometric signal with the concentration of RF showed linearity in a concentration range of 0 to 11  $\mu\text{M}$  with  $R^2 = 0.9973$  and a detection limit of 0.025  $\mu\text{M}$ . The developed nanosensor showed good selectivity over other possible types of interference. The sensor was then applied for the determination of RF in beverage samples using the standard addition method with recoveries between 96% and 106%. Preliminary cytocompatibility tests carried out with breast cancer cells (MDA-MB-231) revealed the nanosensor to be cytocompatible in its working concentration regime, even after long incubation times with cells. Altogether, the developed RF determination method was found to be fast, low-cost, highly sensitive, and selective and can be extended to other samples of interest in the biological and food sectors. Moreover, thanks to its long-lasting cytocompatibility, the developed platform can also be envisaged for other applications of biological interest, such as intracellular sensing and staining for live cell microscopy.

**Keywords:** carbon dots; FRET efficiency; ratiometric fluorescent sensor; donor concentration; RF in beverages; cytocompatible conjugate CDs-RF

## 1. Introduction

Carbon is a black material, insoluble in water, with a weak fluorescence. However, the properties of this material can change dramatically when carbon structures are synthesized



## Results of excisional surgical treatment for mucoceles of the oral cavity: a retrospective study.

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**ABSTRACT:** The mucocele is a lesion that appears in the oral mucosa after a rupture of the duct of a minor salivary gland that spills the mucin into the surrounding soft tissues. The most frequent cause of this retentive lesion is local trauma and the most common is that they require surgical treatment with a prophylactic radical margin of the minor salivary glands close to it. This study was carried out to describe the clinical results of excisional surgical treatment of intraoral mucoceles in the population of Mexicali, Baja California. A retrospective descriptive observational study was carried out with the information of 40 patients diagnosed with a mucocele and operated on in the Oral Surgery service of the Mexicali School of Dentistry, Baja California; between July 2016 and June 2020. These oral lesions were more frequent in women (57.5%) than in men (42.5%), between the ages of 21 and 30, and predominated in students. Only 45% identified a traumatic origin of their injury and less than 25% of the patients had a history of toxic habits. The lower lip was the most affected anatomical site, with no differences between the right and left hemilabium. All patients received surgical treatment, with histopathological confirmation of total excision (95%) and partial excision (5%); and there was only one case that reported recurrence, which represented 2.5%. Excisional surgical treatment was confirmed to have a high level of success.

**KEYWORDS:** Oral mucocele, Mucus retention cyst, Minor salivary gland, Surgical therapy, Epidemiology

### I. INTRODUCTION

The mucocele of a minor salivary gland is a cavity formed in the connective tissue

surrounding it, which can be lined by granulation tissue or epithelium, and which always contains mucus or mucous fluid accumulated inside.<sup>1,2,3</sup>

Etiologically, mucoceles occur due to traumatic or obliterative causes that produce a phenomenon of mucosal extravasation and retention of it. Faced with the extravasation or leakage of saliva out of the duct into the subcutaneous cellular tissue, this lesion mainly manifests as an accumulation of mucin in the extravascular space, due to the rupture of the excretory duct of the minor salivary gland due to some type of trauma and thus it is considered 95% of mucoceles. On the other hand, these lesions can occur due to the presence of a mucous plug, sialolith, or another mechanism that prevents salivary fluid from escaping, causing distension of the minor gland and forming a cavity lined by epithelium.<sup>3-6</sup>

Clinically, mucoceles are limited retentive lesions, which can measure 1 cm or more in diameter, without exceeding 2 cm. The clinical appearance depends on its location and depth, they generally appear as a rounded formation, covered by healthy mucosa, which creates a bluish relief when it is located superficially and has a coral pink color if it is found towards deeper tissue planes. They can be found on all surfaces of the oral mucosa where there are minor salivary glands, with similar conditions: asymptomatic, with slow and progressive growth, not painful and that can interfere with chewing or speech.<sup>2,5-8</sup>

Regarding the epidemiology of mucoceles, the literature indicates that the prevalence of mucocele is 2.5 per 1000 inhabitants in the North American population, and the lower lip is the most affected anatomical area. Although they can appear at any time in life, these lesions of the minor salivary glands usually appear especially



## Retrospective epidemiological study of focal fibrous hyperplasia in the population of Mexicali, Baja California, Mexico.

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**ABSTRACT:** Focal fibrous hyperplasia is a fibrous connective tissue reaction that arises in response to chronic irritation, containing abundant collagen-like scar tissue. This lesion is associated with persistent traumatic factors on oral soft tissues and the treatment of choice is local excision, since they do not regress spontaneously. In the clinical reports of the Mexicali School of Dentistry, focal fibrous hyperplasia is the lesion with the greatest need for histopathological study; For this reason, the following investigation was carried out to determine the epidemiological situation of focal fibrous hyperplasias in the population of Mexicali, Baja California, as well as to specify the most frequent demographic, clinical and histopathological characteristics, and the evolution to surgical treatment. A retrospective descriptive observational study was carried out with the clinical records of 56 patients with histopathological diagnosis of focal fibrous hyperplasia, operated on the Oral Surgery Service of the Mexicali School of Dentistry, Baja California; between January 2018 and December 2019. Epidemiologically, the injuries were more frequent in women (64.3%) than in men (35.7%), in ages from 21 to 40 years, and predominated in housewives. The most common risk factor was occlusal trauma. The most affected anatomical sites: the lower lip (28.6%), the cheek mucosa (25%) and the tongue (16.1%). The excision of the lesion was the biopsy method and surgical treatment in all the patients, which showed a favorable evolution and there was no recurrence of the lesion in any of the cases.

**KEYWORDS:** Fibroma, Gingival Hyperplasia, Focal Epithelial Hyperplasia

### I. INTRODUCTION

Focal fibrous hyperplasia is the most common swelling lesion of the oral cavity that has a reactive origin caused by chronic trauma to the oral mucosa. In these lesions, fibrous connective tissue repair occurs in an exuberant manner, resulting in a clinically evident submucosal mass, covered by healthy mucosa and with almost no symptoms.<sup>1-3</sup>

It is a proliferating lesion of the fibrous connective tissue that arises in response to a chronic irritation that can appear on the lips, gums, the mucosa of the cheeks, the tongue, and the palate. It is observed as a submucosal growth with a smooth surface, it is pink colour or slightly paler than the surrounding mucosa; although it may appear bluish-pink in colour, firm in consistency and sometimes with a sessile or pedunculated base, in them there is an abundant production of collagen, which is why it resembles scar tissue.<sup>4-8</sup>

It is associated with persistent physical irritation of oral soft tissues and is the most common nodular swelling of the oral cavity. They have different etiologies, the most common being chronic and persistent local trauma to the same area of the oral soft tissues. misadjusted prostheses, teeth with sharp edges or restorations, traumatic habits, trauma caused by fixed orthodontic appliances and everything that implies direct physical damage is considered to be the cause of these injuries, they have also been related to excessive consumption of tobacco and / or alcohol.<sup>2, 9-12</sup>

The diagnosis of focal fibrous hyperplasia begins with the clinical method, where the patient reports a history of chronic traumatic irritation and the slow and progressive growth of these lesions. Then, after a very simple surgical procedure, which almost always consists of excisional biopsy, the diagnosis is completed with the histopathological study.<sup>13-16</sup> The clinical and epidemiological presentation tends to confuse them with other very similar neoplastic and non-neoplastic growths.



# CTNNB1 and APC mutations in odontogenic carcinoma with dentinoid

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The purpose of the present study is to report 2 cases of odontogenic carcinoma with dentinoid, a rare low-grade odontogenic carcinoma associated with facial deformity and bone loss, and to investigate the presence of pathogenic mutations in these samples. By using a next-generation sequencing approach, we sequenced a panel of 50 oncogenes and tumor suppressor genes commonly mutated in human cancer. Microscopic features of both cases revealed solid areas of malignant odontogenic tumor with a large amount of dentinoid material. We identified pathogenic mutations in the genes *CTNNB1* and *APC*, both of which are part of the Wnt-signaling pathway. Consistent with Wnt-signaling activation, both tumors showed strong  $\beta$ -catenin accumulation in the cytoplasm and in the nuclei. The molecular profile of odontogenic carcinoma with dentinoid may help in its diagnosis, as well as in the identification of potential molecular targets for therapy in the future. (Oral Surg Oral Med Oral Pathol Oral Radiol 2020;129:e249–e256)

Odontogenic carcinoma with dentinoid (OCD) is a rare low-grade odontogenic carcinoma that is histopathologically characterized by the presence of cords and sheets of epithelial cells with eosinophilic, pale, or clear cytoplasm associated with dentinoid material in a slightly or mature myxoid connective stroma.<sup>1,2</sup> OCD has variable proliferative index but is locally destructive and may exhibit perineural invasion.<sup>3</sup>

The epithelium in OCD does not produce buds or enamel organ-like structures, such as those found in ameloblastic fibrodentinoma, and this tumor does not contain a mesenchymal-like connective tissue resembling dental papilla, as observed in several mixed odontogenic tumors.<sup>3</sup> We identified 9 reported cases fitting the OCD histopathologic criteria, and mean age at diagnosis was the fourth decade of life, with 6 cases reported in the mandible and 6 in the maxilla.<sup>3</sup> All cases showed evidence of tumor infiltration into adjacent tissues and deposits of dentinoid material.<sup>1–7</sup>

In 2017, the World Health Organization classification of odontogenic and maxillofacial bone tumors included 5 types of odontogenic carcinomas, 1 odontogenic carcinosarcoma, and 1 odontogenic sarcoma.<sup>8</sup> However, this classification did not recognize other malignant odontogenic tumors that may produce dentinoid.

Here, we report 2 cases of OCD that we received for consultation. All data from these cases were retrospectively retrieved. In addition to reporting the cases, we discuss their molecular profile, as revealed by next-generation sequencing (NGS) of a panel of cancer-associated genes.

## CASE REPORT

### Case 1

A 43-year-old man presented with a painless slow growing mass in the anterior part of the left maxilla, measuring 5 × 4 cm. The patient had a previous history of tumor resection in the same area 2 years earlier. Computed tomography scan revealed that the tumor had invaded the nasal cavity and the maxillary sinus (Figure 1A) and had well-defined limits with no mineralized tissue deposition. According to the pathologic report of the first surgery, the diagnosis was of pleomorphic adenoma. With the clinical diagnosis of recurrent benign tumor, the patient underwent left maxillectomy. A histopathologic diagnosis of malignant odontogenic tumor was reached, and the patient was referred to an oncologist and underwent radiotherapy and chemotherapy, but no information about the regimen could be retrieved. The patient has been followed up for 24 months without evidence of recurrence.

After the diagnosis of malignant odontogenic tumor, the case was referred to us for consultation. Microscopic examination of the tumor revealed solid proliferation of polyhedral, basaloid, and clear cells, forming

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## Is periodontal disease a risk factor for severe COVID-19 illness?

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### ARTICLE INFO

#### Keywords:

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Periodontal disease  
Risk factors  
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### ABSTRACT

Periodontal disease (PD) comprises a group of diseases involving inflammatory aspects of the host and dysbiotic events that affect periodontal tissues and could have systemic implications. Diverse factors and comorbidities have been closely associated with PD such as diabetes, obesity, aging, hypertension, and so on; although, underlying mechanisms or causal associations have not been established completely. Interestingly, these same factors have been widely associated with progression or severe coronavirus disease 2019 (COVID-19), an illness caused by coronavirus SARS-CoV-2. Since inflammatory and dysbiotic factors as well as comorbidities affect systemic health, it is possible that periodontal status indicates the risk of complication of COVID-19. However, assessment of oral health history including periodontal status in COVID-19 patients has not been reported. Knowing PD is associated with severe COVID-19 could help identify risk groups and establish pertinent recommendations.

### Introduction

Periodontal diseases are a group of chronic inflammatory diseases, including gingivitis and periodontitis [1–3]. These diseases are driven by several microbial agents that cause inflammation and destruction of tooth-supporting tissues [4]. According to the World Health Organization (WHO), PD affects 10% of the global population [5]. Poor oral hygiene, tobacco smoking, diabetes, medication, age, hereditary, and obesity have been related to increasing the risk of PD [6–8]. Similarly, other studies suggest the association between PD and other diseases such as diabetes, hypertension, asthma, liver diseases, among others [9–11].

COVID-19 is a disease caused by novel coronavirus named SARS-CoV-2 that triggers damage to the lungs and other organs [12]. Most COVID-19 patients present mild symptoms; however, a few could develop severe illness having pneumonia, pulmonary edema, acute respiratory distress syndrome (ARDS), multiple organ dysfunction syndrome, or even die [13]. There are other diseases like severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS) by other coronaviruses that cause respiratory problems [12,14]. COVID-19 was declared a pandemic by the WHO on March 11th. At present, in May 2020, there are more than 3,000,000 infected people around the world. Of all infected, only a small percentage induces critical state, considering the presence of any comorbidity or

condition, which can be diabetes, hypertension, obesity, asthma, pregnancy, lung diseases, liver diseases, oral dysbiosis, aging, and gender [12,15,16].

This work proposes to evaluate if PD could be a risk factor for developing severe COVID-19 illness because of shared risk factors.

### Hypothesis

PD could be associated with severe COVID-19 illness. Oral medical history of PD could be a characteristic to identify a risk group to severe COVID-19. The suggested relationship between PD and severe COVID-19 illness could be connected to closely shared risk factors among these affections. Most comorbidities and risk factors reported in patients with severe COVID-19, also aggravate the development of PD. Until now, information on oral health history including periodontal status in patients with severe COVID-19 illness has not been reported.

### Evaluation of hypothesis: Shared risk factors by PD and severe COVID-19 illness

#### Aging

Aging is considered a process that causes degenerative changes at the cellular level and sometimes leads to various diseases that can be

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## Article

# TIE2 Induces Breast Cancer Cell Dormancy and Inhibits the Development of Osteolytic Bone Metastases

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**Abstract:** Breast cancer (BCa) cells disseminating to the bone can remain dormant and resistant to treatments for many years until relapsing as bone metastases. The tyrosine kinase receptor TIE2 induces the dormancy of hematopoietic stem cells, and could also induce the dormancy of BCa cells. However, TIE2 is also a target for anti-angiogenic treatments in ongoing clinical trials, and its inhibition could then restart the proliferation of dormant BCa cells in bone. In this study, we used a combination of patient data, in vitro, and in vivo models to investigate the effect of TIE2 in the dormancy of bone metastases. In BCa patients, we found that a higher *TIE2* expression is associated with an increased time to metastases and survival. In vitro, TIE2 decreased cell proliferation as it increased the expression of cyclin-dependent kinase inhibitors *CDKN1A* and *CDKN1B* and arrested cells in the G<sub>0</sub>/G<sub>1</sub> phase. Expression of *TIE2* also increased the resistance to the chemotherapeutic 5-Fluorouracil. In mice, *TIE2* expression reduced tumor growth and the formation of osteolytic bone metastasis. Together, these results show that TIE2 is sufficient to induce dormancy in vitro and in vivo, and could be a useful prognostic marker for patients. Our data also suggest being cautious when using TIE2 inhibitors in the clinic, as they could awaken dormant disseminated tumor cells.

**Keywords:** breast cancer; bone metastasis; dormancy; TIE2; chemotherapy resistance; cancer relapse

## 1. Introduction

Breast cancer (BCa) is the most common cancer in women worldwide [1]. BCa cells have a propensity to home to the bone, causing bone metastases in at least 75% of patients with advanced-stage BCa [2]. The development of these bone metastases can occur years or decades after the treatment of the primary tumor [3]. During this time, although patients appear to be cancer-free, disseminated tumor cells (DTCs) are lodged in their bone marrow, where they remain in a stage of dormancy [4]. Cellular dormancy is characterized by reduced metabolism and cell growth arrest that



## Article

# Lipid Modulation in the Formation of $\beta$ -Sheet Structures. Implications for De Novo Design of Human Islet Amyloid Polypeptide and the Impact on $\beta$ -Cell Homeostasis

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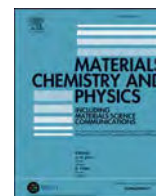
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**Abstract:** Human islet amyloid polypeptide (hIAPP) corresponds to a 37-residue hormone present in insulin granules that maintains a high propensity to form  $\beta$ -sheet structures during co-secretion with insulin. Previously, employing a biomimetic approach, we proposed a panel of optimized IAPP sequences with only one residue substitution that shows the capability to reduce amyloidogenesis. Taking into account that specific membrane lipids have been considered as a key factor in the induction of cytotoxicity, in this study, following the same design strategy, we characterize the effect of a series of lipids upon several polypeptide domains that show the highest aggregation propensity. The characterization of the C-native segment of hIAPP (residues F<sub>23</sub>-Y<sub>37</sub>), together with novel variants F<sub>23</sub>R and I<sub>26</sub>A allowed us to demonstrate an effect upon the formation of  $\beta$ -sheet structures. Our results suggest that zwitterionic phospholipids promote adsorption of the C-native segments at the lipid-interface and  $\beta$ -sheet formation with the exception of the F<sub>23</sub>R variant. Moreover, the presence of cholesterol did not modify this behavior, and the  $\beta$ -sheet structural transitions were not registered when the N-terminal domain of hIAPP (K<sub>1</sub>-S<sub>20</sub>) was characterized. Considering that insulin granules are enriched in phosphatidylserine (PS), the property of lipid vesicles containing negatively charged lipids was also evaluated. We found that these types of lipids promote  $\beta$ -sheet conformational transitions in both the C-native segment and the new variants. Furthermore, these PS/peptides arrangements are internalized in Langerhans islet  $\beta$ -cells, localized in the endoplasmic reticulum, and trigger critical pathways such as unfolded protein response (UPR), affecting insulin secretion. Since this phenomenon was associated with the presence of cytotoxicity on Langerhans



# Magnetic nanocomposite with fluorescence enhancement effect based on amino acid coated-Fe<sub>3</sub>O<sub>4</sub> functionalized with quantum dots

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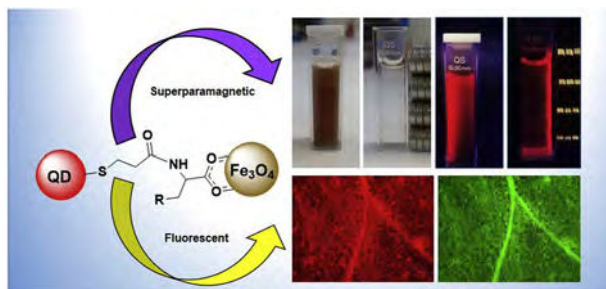
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## HIGHLIGHTS

- QDs were successfully linked to AA coated-Fe<sub>3</sub>O<sub>4</sub> magnetic nanoparticles via covalent bond.
- AA are a robust anchor for binding QDs on the Fe<sub>3</sub>O<sub>4</sub> surface.
- Fe<sub>3</sub>O<sub>4</sub>@AA@QDs presents high stability, good dispersibility in water and excellent magnetic and fluorescent properties.
- Fe<sub>3</sub>O<sub>4</sub>@Trp@QDs showed a fluorescence enhancement effect due to FRET process.
- The nanocomposite has great potential as a fluorescent nanoplatform for sensing and imaging.

## GRAPHICAL ABSTRACT



## ARTICLE INFO

### Keywords:

Magnetic and fluorescent nanocomposite  
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Amino acid as anchor  
Fluorescent enhancement  
Energy transfer  
Stability and dispersibility in water

## ABSTRACT

Multifunctional nanoparticles with magnetic and fluorescent properties have high potential in different areas. A very attractive feature of these nanoparticles is that they can be controlled by an external magnetic field and monitored by fluorescence. For biological applications, the magnetic nanoparticles (MNPs) must be biocompatible and dispersible in water, which requires surface modification. This paper describes the synthesis of Fe<sub>3</sub>O<sub>4</sub> MNPs modified with three amino acids (AA): L-Tryptophan (Trp), L-Phenylalanine (Phe) and L-Tyrosine (Tyr) by a co-precipitation method in a one-step reaction without the use of a spacer agent. The potential of AA as a robust anchor was assessed by binding mercaptopropionic acid (MPA)-coated CdTe quantum dots (QDs) to Fe<sub>3</sub>O<sub>4</sub>@AA nanoparticles, leading to a hybrid nanostructure with excellent fluorescent and magnetic properties. In

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# ***Bacillus subtilis*, an ideal probiotic bacterium to shrimp and fish aquaculture that increase feed digestibility, prevent microbial diseases, and avoid water pollution**

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## **Abstract**

Beneficial microorganisms maintain the ecosystems, plants, animals and humans working in healthy conditions. In nature, around 95% of all microorganisms produce beneficial effects by increasing nutrients digestion and assimilation, preventing pathogens development and by improving environmental parameters. However, increase in human population and indiscriminate uses of antibiotics have been exerting a great pressure on agriculture, livestock, aquaculture, and also to the environment. This pressure has induced the decomposition of environmental parameters and the development of pathogenic strains resistant to most antibiotics. Therefore, all antibiotics have been restricted by corresponding authorities; hence, new and healthy alternatives to prevent or eliminate these pathogens need to be identified. Thus, probiotic bacteria utilization in aquaculture systems has emerged as a solution to prevent pathogens development, to enhance nutrients assimilation and to improve environmental parameters. In this sense, *B. subtilis* is an ideal multifunctional probiotic bacterium, with the capacity to solve these problems and also to increase aquaculture profitability.

**Keywords** Probiotics · *Bacillus subtilis* · Pathogenic bacteria · Aquaculture · Profitability

## **Overview**

Seafood always has been an excellent source of proteins, lipids, carbohydrates, vitamins, minerals, and essential micronutrients; however, fisheries capture has been decreasing for the last 20 years (FAO 2006). In this sense, aquaculture systems are gaining social, environmental, and economic importance around the world. However, aquaculture diets contain fish protein and fish oil inducing oceans fish imbalance, increase animals feeding cost and generate ponds contamination (Tacon and Metian, 2008; Olmos

et al. 2015). Ponds contamination produces an imbalance in environmental parameters that immunocompromise the animals, induce pathogens proliferation and consequently the organism's death (Merrifield et al. 2010; Stentiford et al. 2012; Tran et al. 2013). Thus, proteins, carbohydrates and complex lipids (PCL) from grains (soybean, corn, wheat and sorghum) are increasingly common in shrimp and fish aquaculture to reduce feeding cost and to prevent ponds contamination (Olmos et al. 2011; Lopez et al. 2016). However, neither shrimp nor marine fishes produce enzymes to digest complex PCL contained in grains, which increase feed losses, ponds contamination and enhance viral and bacterial diseases (Olmos and Paniagua 2014; Olmos 2017). In this sense, *B. subtilis* can grow in almost any carbon and nitrogen source, because its enzymes break down proteins, carbohydrates and complex lipids from animal and vegetable origin (Sonnenschein et al. 1993; Arellano and Olmos 2002; Ochoa and Olmos 2006; Cui et al. 2018). *B. subtilis* enzymes could prevent diseases by improving water quality through ponds bioremediation (Olmos et al. 2011; Zorriehzakra et al. 2016). In addition, good relationship has been established by a long period of time between *B. subtilis* and the animal's immune system (Cutting, 2011; Huang et al.

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# Fatty acid synthase and Ki-67 immunoexpression can be useful for the identification of malignant component in carcinoma ex-pleomorphic adenoma

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**Background:** Fatty acid synthase (FASN) is the key molecule for catalyzing fatty acid synthesis and have been associated with several malignant tumors.

**Methods:** We analyzed the expression of FASN and Ki-67, by immunohistochemistry on 29 carcinomas ex-pleomorphic adenoma (CXPA) and 25 pleomorphic adenomas (PAs).

**Results:** Ki-67 proliferation index and FASN expression were significantly higher in patients with CXPA than patients with PA ( $P < 0.001$ ). We found intense immunoreactivity for FASN in the malignant component of CXPA, and these malignant areas also had intense nuclear immunoreactivity for Ki-67.

**Conclusions:** The present results suggest that overexpression of FASN in CXPA might be associated with malignant transformation of ductal epithelial cells and/or myoepithelial cells from PA. FASN associated with Ki-67 may be useful diagnostic markers for CXPA.

## KEYWORDS

fatty acid synthase, salivary gland tumors, tumor cell proliferation

## Solitary xanthoma affecting the oral mucosa: Immunohistochemical analysis and literature review

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### BRIEF COMMUNICATION



## Solitary xanthoma affecting the oral mucosa: Immunohistochemical analysis and literature review

### 1 | INTRODUCTION

Xanthomas are microscopically characterized by localized infiltrates of lipid-laden macrophages, usually on the skin and mucosal surfaces (respiratory and gastrointestinal tracts).<sup>1-8</sup> Cutaneous xanthoma in particular may represent a localized idiopathic phenomenon or systemic hyperlipidemia.<sup>3</sup> While several types of cutaneous xanthomas have been described in the literature,<sup>1,2</sup> those affecting the respiratory and gastrointestinal tracts are usually named "xanthomas."<sup>3-8</sup> Recent studies have also reported xanthomas at intraosseous locations, affecting the jaws.<sup>9-11</sup>

Interestingly, xanthomas, as described in the respiratory and gastrointestinal tracts,<sup>3-8</sup> have not been reported in the oral mucosa. Here, we report an oral lesion containing microscopically a prominent

proliferation of xanthomatous cells, diagnosed as xanthoma. Other conditions such as juvenile xanthogranuloma (JXG) and verruciform xanthoma (VX) should be considered in the clinicopathological differential diagnosis.

### 1.1 | Case report

A 46-year-old woman presented with an asymptomatic lip lesion that had developed over several weeks. The patient medical history was non-contributory, and nothing remarkable was found during physical examination, especially on the skin, joints, and mucosal surfaces other than mouth. Intraoral examination revealed a yellowish ovoid nodule on the mucosal surface of the upper lip, with a slightly rough surface.