RESULTS: The patient showed no complications of any kind either perioperatively or postoperatively. There was no postoperative bleeding and no malignant hyperthermia crisis occurred.
CONCLUSIONS: The odontostomatological treatment of the patient with Steinert's dystrophy must be carried out in a protected regime and the use of local anesthetic without vasostrittor, anxiolysis and with the constant presence of dantrolene sodium is advisable given the possibility of triggering a malignant hyperthermia crisis due to surgical stress.

Bioinformatic and immunohistochemical analyses of BIRC5/survivin expression in oral squamous cell carcinoma

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BACKGROUND: Survivin is a well-known protein involved in the inhibition of apoptosis in many different cancer types. Bioinformatics analysis focused on genetic mutations, mRNA expression, methylation and gene network. In addition, immunohistochemistry analysis from a single institution database was performed in order to study the prognostic significance of cytoplasmic and nuclear expression of survivin in OSCC. The aim of this study was to perform an integrate bioinformatic and histologic analysis in order to study the role of survivin and its related gene BIRC5 in OSCC.
METHODS: The expression level of the BIRC5 mRNA in OSCC samples compared to normal tissue was analyzed through Oncomine gene expression array datasets (https://www.oncomine.org/). In addition, the gene expression profile of two published databases (GSE85195 and GSE10121) were downloaded from Gene Expression Omnibus (GEO) using the GEO2R platform (https://www.ncbi.nlm.nih.gov/geo/geo2r/). In addition raw data from The Cancer Genome Atlas (TCGA) were also obtained in order to analysis: the rate of mutations, gene expression and methylation in patients with oral squamous cells carcinoma (OSCC). Immunohistochemistry (IHC) was also performed, on a Tissue Micro Array (TMA) of a single institution, in order to evaluate the nuclear and cytoplasmic expression of Survivin in samples from OSCC patients.
RESULTS: Data from this study revealed that Survivin is rarely mutated in OSCC samples, and is upregulated compared to non-cancerous tissue. Data from the TCGA database revealed that BIRC5 gene expression is an independent prognostic factor for OSCC. Analysis of the network revealed that: CDKN2a, MYC and FOXM1 control the expression of BIRC5, while: AKT1-3, PRCACA, BUB1 and CSNK2A1 controls a reaction that changes the state of the survivin protein (Figure 3). Correlations analysis between BIRC5 mRNAs expression, methylation and clinicopathologic parameters of patients with OSCC revealed a significance inverse correlation between the methylation and the mRNA expression of BIRC5, in addition mRNA expression correlated with the stage of the disease. In addition, IHC staining revealed that cytoplasmic but not nuclear expression of Survivin correlates with a poor overall survival in OSCC patients.
CONCLUSIONS: Aggregate bioinformatic and immunohistochemical analysis revealed that survivin is overexpressed both at mRNA and protein level. In addition, it represents an independent prognostic factor in patients with oral squamous cell carcinoma.

PD-L1 expression in oral squamous cell carcinoma microenvironment and prognostic correlations

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BACKGROUND: Tumor Microenvironment stands for the complex organization and pool of different cell types that are able to produce different molecules, which take part in different cellular mechanisms, such as cell growth and metastasis. Tumor Associated Macrophages (TAM) seems to be involved in increase of survival cells, angiogenesis and metastasis, leading to a poorer prognosis. Recently, different studies showed the importance of PD1-PDL1 interaction in the therapy of different cancers. PD1 (Programmed Death 1) is usually expressed on the extracellular side of the T-cell membrane. In many cases, PD-L1 has been showed to be overexpressed on the surface of tumoral cells. The interaction between PD1/PD-L1 leads to a T cell dysfunction, decreasing the immune response against the cancer cells. Nivolumab and Pembrolizumab, are monoclonal antibodies directed against the Programmed Cell Death Protein 1 (PD-1) receptor. They both showed a therapeutic benefit in different kinds of cancer. Anyway, in one hand, it has emerged that not all PD-L1-expressing tumors respond to PD-1/PD-L1 inhibitors. On the other hand, PD-L1-negative tumors can respond to these agents (Aguiar et al. 2016). Backgroun of this study is to investigate the PD-L1 expression in the Microenvironment of Oral Squamous Cell Carcinoma (OSCC) samples and its correlation to prognostic data.
METHODS: Three paraffine recipient blocks for Tissue Micro Array (TMA) were constructed by coring 44 paraffine donor blocks. The HPV status was assessed by performing In Situ Hybridation (ISH) using probes for HR-HPVs 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, e 66 (Inform HPV family-III 16 Probe; Ventana - Roche) and s for LR-HPVs, 6, 11 (Inform HPV famly-II 6 Probe; Ventana – Roche). Immunohistochemistry (IHC) to detect PD-1 and PD-L1 expression was performed on consecutive 4-micron sections by using Ventana Benchmark® autostainer using rabbit monoclonal anti-PD-L1 clone SP142 and PD-1 (NAT105) by Ventana-Roche. Every 0,6 mm core section has been evaluated for degree of lymphoid cell infiltration surrounding the tumor nests, according to Wada grading system [Wada T. et al. Nature of monoclonal cell infiltrates in oral squamous cells carcinoma and its clinical significance Wakayama Med Rep 30: 103-117. 1989]. Tumor-infiltrating lymphocytes (TILs) was identified by morphology. PD-1, PD-L1 IHC expression has been assessed in tumor cells and inflammatory cells evaluating the intensity of stain. Statistical analysis was performed by using SPSS.Ink Software v.20.
RESULTS: Kaplan-Meier Univariate Analysis showed correlation between presences of tumor associated lymphocytes (TIL) and better survival data (p=0,024). We observed positivity for PD-L1 tumor cells in 8 cases on 38 cases that were evaluable, 21% of total cases, against a mean of 60% in literature. This data was not significant in any association. Kaplan-Meier Univariate Analysis showed correlation between the presence of macrophages and better prognosis in patients (p=0,008) Hazard Ratio=0,092 (CI 95% 0,009-0,926). We observed a correlation between PD-L1 negative macrophages and a worst prognosis. This data was near Statistical significance p=0,054.
CONCLUSIONS: Different studies showed a different

pattern of expression of PD-L1 in different cell types associated to the tumor, highlighting the differences in therapeutic response. A better understanding of PD-1/PD-L1 expression in the different cell types involved in the tumor environment should be the new aim of next studies, for a better understanding of this molecular process and the selection of patients, which could undergo new immune therapies.

Relevance of hypovitaminosis D in the etiopathogenesis of periodontitis in special needs patients

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BACKGROUND: The aim of this review is to focus on the probable correlations between Periodontitis due to Phorphyromonas gingivalis, pro-inflammatory cytokines and Hypovitaminosis D associated to several systemic diseases such as Hepatitis B and C, Morb of Crohn and Celiac Disease.
METHODS: It proceeded with the review of the literature on the search engine PUBMED/MEDLINE, combining the keywords "Hypovitaminosis D", "Systemic Diseases" and "Periodontitis". The selection criteria were articles conducted in vitro or in clinical trial mode on humans.
RESULTS: Periodontitis is not directly caused by P. gingivalis infection but has a multifactorial etiology and is associated after inflammation with the adherence and colonization of pathogenic bacteria on the gingival epithelium. The importance of Vitamin D is that reduces periodontitis related to Phorphyromonas gingivalis by the inhibition of IL-8 expression in periodontal ligament cells (Tang et al). What is more, also IL-10 might be involved in the repair of periodontal tissue (Goutoudi et al.). Many studies suggest that 1,25(OH)2D3 improved the expression of IL-10 that might suppress the inflammatory response, promote the repair of periodontal tissue, and reduce immune-associated injury to periodontal tissue. DBP was measured in the GCF and plasma of patients with GAgP but without systemic disease. It was found that patients with GAgP had lower GCF DBP concentrations (Xin Zhang et al). The aim of this cross-study was to underline that many systemic diseases can lead to vitamin D or DBP deficiency that can involve to a predisposition to Periodontitis. Celiac disease leads to an altered intake of Calcium or Vitamin D, but it has also been hypothesized (Sadeghian at Al. 2016) that Crohn's disease leads to a deficit of the same micronutrient. Being DBP is an alpha-globulin it is synthesized by the liver and therefore its deficit is resistant to all hepatic diseases such as cirrhosis, hepatitis B and C. Therefore all these diseases can indirectly favor the presence of severe periodontitis. In these patients, subsequent studies could focus on topical administration of deficient micronutrients. In this way it could be possible to modulate the action of P. Gingivalis and in general of many cytokines that act negatively on inflammation.
CONCLUSIONS: Since periodontitis is a multifactorial disease it is very difficult to investigate the correlation between hypovitaminosis D, systemic diseases and oral manifestations of this. More cross studies are needed to clarify how all these factors can affect oral health.

Salivary biomarkers for diagnosis of cardiovascular disease: a systematic review

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BACKGROUND: Cardiovascular disease (CD) is the first cause of death for disease, approximately 17.3 million people per year in the world. The global prevalence of this group of diseases has been 422,7 million in 2015. CD has a terrific economic impact, on the basis of costs for diagnosis and therapy, early death of patients and disability. It has been estimated a total amount of expenses of around 400 billion of dollars for year. Apart the development of traditional diagnostic approaches for CD, alternative methods have gained interest in the last year. Among these salivary diagnostics if rapidly gaining popularity. Saliva is a complex fluid, easy to transport and store, non-invasive to collect, and it reflects somehow blood composition. Several molecules dispersed in saliva can be used as diagnostic and prognostic biomarkers for a wide range of diseases. The aim of the present systematic review is to define if there is scientific evidence to support the role of salivary biomarkers for diagnosis of CD.
METHODS: We searched into Medline, Scopus and Web of Science databases using as entry terms the combination of "saliva" with "diagnosis", "systemic disease", "biomarkers", "cardiac disease", "heart", "myocardial infarction" and "coronary disease". We included only studies in English and published after 2000. We considered only studies on saliva sample, addressing CD, and evaluating biomarkers for diagnosis. We excluded studies on animals or *in vitro* samples and papers dealing with systemic microbial infections, hormones, drugs dosage. Research investigating correlation between CD and periodontal disease were not considered. References listed in reviews, were screened in order to identify papers possibly missing from the database search. Information extracted included title, Authors, publication year, type of biomarker, biochemical method and device used to analyse saliva. Quality of studies was assessed according to the guidelines of the National Institute of Health (NIH - scores ranging from "poor" to "good").
RESULTS: Starting from a total amount of 18348 records, we selected 13 studies meeting inclusion and exclusion criteria Two more papers were identified through the screening of the reference lists of five reviews. One article was excluded because concerning the state-of-art of devices for detecting molecules in cardiopatic patients. Eventually, 14 papers were took into consideration for inclusion in the present review. In all studies biomarkers were proteins. Twelve out of 14 papers reported statistically significant results of association between CD and biomarkers. Following the NIH quality assessment, twelve articles were scored as "fair quality" (85%) and two articles as "good quality" (15%). No one of the papers included was considered as having "poor quality".
CONCLUSIONS: The use of saliva as a diagnostic tool seems to be a realistic possibility for the diagnosis of CD. Most of the articles evaluated here showed statistically significant results.
The future for research should include the sensibility and specificity of methods and devices used in salivary diagnostics.