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Letter to the Editor

Correlation of chronic periodontitis progression with sTREM-1 and E-Cadherin salivary levels

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To the Editor,

Chronic periodontitis is a common infectious disease in humans, caused by periodontopathic bacteria, which untreated can lead to destruction of tooth supporting tissues and eventually tooth loss (1). It is the consequence of an imbalance between the production of host inflammatory mediators, amplified by the presence of periodontal pathogens (2). In a previous study published in your journal, authors demonstrated that the salivary level of the 8-OHdG and IL-1 gene polymorphism can be used in the evaluation of the oro-dental status at patients with aggressive periodontitis (3). We observed two other substances in saliva with possible quality of biomarkers in chronic periodontitis:

TREM-1 is a novel cell surface receptor, which belongs to the immunoglobulin superfamily, with an important role in regulating inflammatory responses against invading bacteria, by increasing cytokine production (4). Increased plasma concentration of TREM-1 has already been demonstrated in patients with septic shock, bacterial and fungal infections (5). Salivary sTREM-1 has already been positively correlated with the presence of periodontal disease, showing a possible role of this molecule as a biomarker (6).

E-Cadherin is a glycoprotein, located on a cell's membrane, with a major role in connecting epithelial cells through adherens junctions (7). In the gingival junctional epithelium E-cadherin is responsible for maintaining its structural integrity and preventing bacterial invasion and a reduction of this molecule was shown in the inflamed gingival tissue, leading to an increased epithelial permeability for periodontopathic bacteria and progression of periodontitis (8). Our pilot study monitorised a possible correlation between salivary levels of sTREM-1 and E-Cadherin during the progression of chronic periodontitis. For this study a total of 79 subjects with a mean age of 54 years were selected (41 females and 38 males). The study was approved by the Ethics Committee of the School of Medicine, *Lucian Blaga* University (Protocol no: 4323/15.05.2015) and was carried out over a period of 5 months. All subjects were recruited from patients visiting the Department of Oral and Maxillofacial surgery of University Hospital of Sibiu, Romania. Inclusion criteria for all subjects - all patients with over 50% of all dental units present, with clinical and radiological signs of chronic periodontitis: gingival bleeding, gingival recession, clinical attachment loss, radiographic bone resorption, periodontal pockets, tooth mobility, migration or tooth loss in advanced stages of the disease. Exclusion criteria were: patients with medical history of cardiovascular, kidney, lung diseases, diabetes mellitus, obesity, osteoporosis, rheumatoid arthritis, cancer, alcoholics and smokers, as well as patients who underwent surgical or non-surgical periodontal treatments within the past 12 months or who underwent any drug therapy over the last 4 months.

Group I: healthy group (HG), included a total of 20 subjects, 11 males and 9 females, with a mean age of 42 years, with no clinical or radiological signs of chronic periodontitis.

Group II: early generalized chronic periodontitis group (EGP) included 13 patients, 6 males and 7 females, with a mean age of 48 years, who

presented clinical attachment loss (CAL) of 1-2 mm, gingival bleeding, dental plaque and bone loss of 2-3 mm of the interdental septum, in more than 30% of the dental sites.

Group III: moderate generalized chronic periodontitis group (MGP) consisted of 23 patients 6 males and 17 females with a mean age of 56 years, with CAL of 3-4 mm, gingival bleeding, dental plaque and radiographic bone resorption of 3-5 mm, but not more than 50% of the radicular length, in more than 30% of the dental sites.

Group IV: advanced generalized chronic periodontitis group (AGP) consisted of 23 patients 15 males and 8 females, with a mean age of 60 years. They presented CAL of 5-6 mm, dental plaque and bone resorption of over 5 mm or over 50% of the radicular length in multiple sites of all 4 quadrants of the mouth.

Medical and dental history was compiled for all patients and clinical parameters were evaluated by the same examiner, after the purpose of the study was explained and informed consent was obtained from each subject. Unstimulated saliva was obtained from donors who abstained from tooth brushing over the last 12 hours and food or drink intake on the same day. The samples were collected between 9-12 am, in sterile Eppendorf tubes. The samples were stored at -40C for further analysis. ELISA test was used

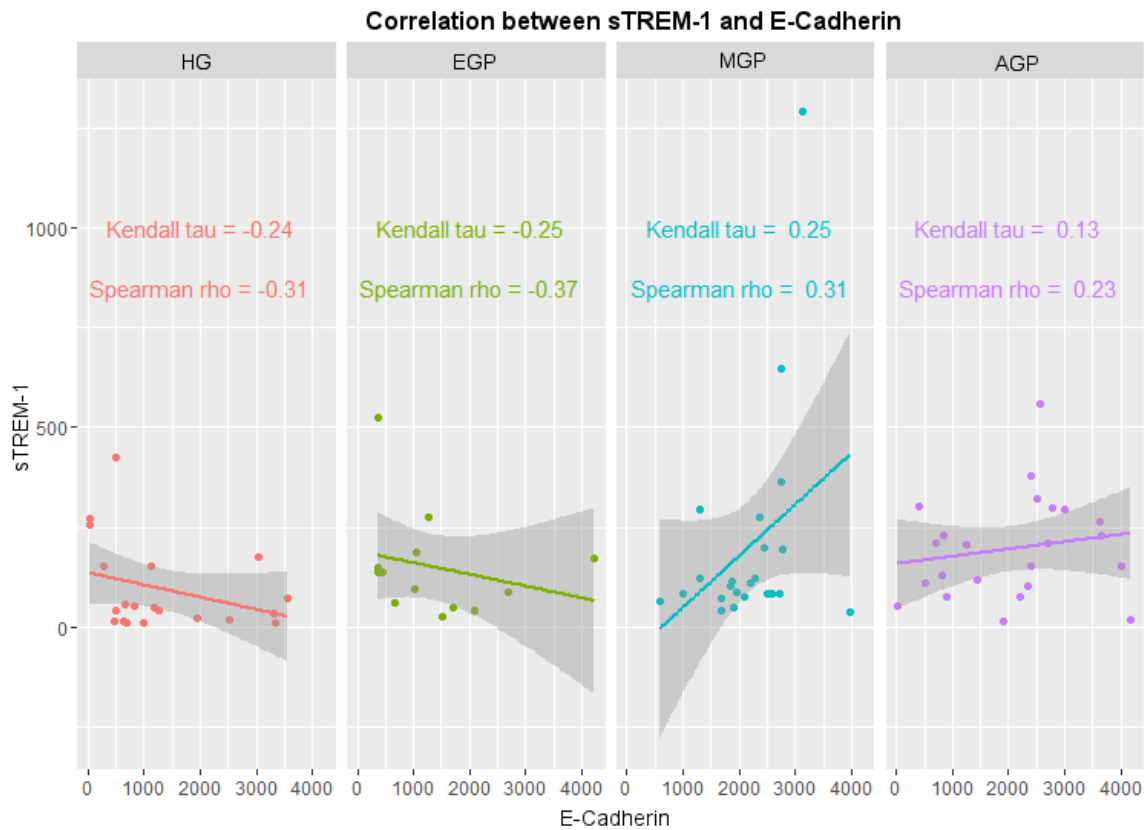

Fig.1 Kendall and Spearman correlation between sTREM-1 and E-Cadherin in healthy group (HG), early generalized chronic periodontitis group (EGP), moderate generalized chronic periodontitis group (MGP) and advanced generalized chronic periodontitis group (AGP).

for quantification of E-cadherin (assay Biotech) and sTREM-1 (Hycult Biotech) in the saliva samples. The detection thresholds for salivary concentrations of sTREM-1 was 31.3 pg / ml and respectively 187.5 pg / ml for E-cadherin.

Statistical analysis was performed using R programming language for data analysis. Non-parametric Spearman and Kendall rank correlation coefficients were used to analyze the statistical dependence between salivary sTREM-1 and E-Cadherin for healthy and chronic periodontitis groups. 95% confidence intervals and p values were calculated and statistical significance was defined at *p* less than 0.05.

To our knowledge there are no other studies that associate salivary levels of sTREM-1 and E-cadherin during the progression of chronic periodontitis. Some studies showed important associations between systemic sTREM-1 levels and the severity of periodontal disease and demonstrated that sTREM-1 is highly correlated with the presence of periodontal pathogens (9). In this study we observed increased concentrations of sTREM-1 in periodontitis subjects compared to healthy ones, although no statistically significant differences could be observed.

E-Cadherin has been studied in the gingival epithelium of subjects with chronic periodontitis and a reduced expression of this molecule was shown in periodontal sites, given the altered function of the epithelial structure to work as a barrier against invasion of periodontal pathogens (10). Our study revealed high salivary levels of E-cadherin in advanced stages of chronic periodontitis. This results might suggest a loss of E-cadherin in the epithelium, causing an increased expression of its soluble form present in the saliva, in patients with periodontal disease. Aiming to determine a correlation between sTREM-1 and E-Cadherin at salivary levels, we were able to establish an interdependence between the two molecules in the 4 groups. Our study shows that salivary levels of sTREM-1 and E-Cadherin vary differently along with progression of periodontal disease. Using Spearman and Kendall rank correlation analysis, we observed a negative interdependence between the two molecules in the HG (Kendall tau=-0.24, Spearman rho=-0.31) and EGP group (Kendall tau=-0.25, Spearman rho=-0.37), however correlations were not statistically significant. While sTREM-1 showed increasing levels, E-Cadherin decreases in the HG as well as in the EGP group. Our study shows that increasing levels of sTREM-1 are associated with reduced expression of E-Cadherin in the HG and EGP group. On the other hand, our analysis showed a positive correlation between sTREM-1 and E-Cadherin variations in the MGP and AGP groups (both of them being decreased). The data suggest a direct relationship between the two molecules in these stages of periodontal disease. Therefore, severity of chronic periodontitis might affect levels of sTREM-1 and E-Cadherin in the same way only in the moderate and advanced stages of the disease. The results were not statistically significant, however they suggest the possibility that an interdependence between these two molecules, in different stages of periodontal disease, might exist.

Salivary sTREM-1 and E-cadherin may serve as possible biomarkers in chronic periodontitis. Chronic periodontitis progression might influence interdependence between the two molecules and their different variations. More homogenous groups and correlations between different biomarkers are required in order to establish a salivary biomarker profile of chronic periodontitis.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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