Ghrelin is a 28-aminoacid peptide, responsible for the appetite stimulation. Its serum levels increase before the meal and decrease around 1h after ingestion, which is being interpreted as the “eat” signal in mammals. The serum levels are mainly maintained by the stomach epithelium, yet ghrelin expression was reported for various tissues, including oral epithelium, where ghrelin is postulated to regulate the development of inflammation, by exerting the anti-inflammatory functions. Ghrelin interacts with GSHR1a receptor and regulates numerous functions throughout the body. Initially it was described as the growth-hormone release stimulating molecule in the pituitary gland, but soon its metabolic functions were described, which include regulation of the food intake, regulation of the insulin release and the fat deposition. Ghrelin was also found to regulate the inflammatory reaction by modulation of the cytokine production in response to LPS and TNF-α stimulation (expression and possible immune-regulatory function of ghrelin in oral epithelium.

Periodontitis is the most prevalent inflammatory conditions in the developed countries, as according to the recent study almost 50% of Americans (age >30) is affected by periodontitis, with almost 10% of citizens suffering from its severe form. In similar fashion, obesity is highly prevalent in United States, where 35% of adults (age >20) was found obese, defined by BMI index >30, according to the recent study. Astonishingly, the high obesity increase rate and high periodontitis diagnosis overlap in the same patients group (Hispanic male and African-descent male). Similarly, the occurrence of overweight and obesity in Europe is estimated as 55% (defined by BMI >25). Periodontitis data are not available for European countries, however as periodontitis prevalence differs 2-fold between lowest and highest socioeconomic status it is expected, that regardless of ethnicity, the poor/less educated citizens will display similar to US (50-60%) fraction affected by periodontitis with no relation to the country of origin or ethnicity.

Porphyromonas gingivalis is a human pathogen included in the “red complex” responsible for the development of periodontitis. This bacteria is well-known to secrete numerous virulence factors, among which gingipains – cysteine proteinases of the caspase-like fold are the main weapon in the arsenal of the bacteria. Gingipains are products of three genes – *rgpA*, *rgpB* and *kgp*. Two former encode arginine-specific proteases with almost identical catalytic domains and differing in the adhesion domain organization, while the latter encodes exclusively Lys-specific proteinase. Together gingipains R (Arg-specific) and K (Lys-specific) constitute 80% of total proteolytic activity and 99% of trypsin-like activity in the culture medium. Interestingly, processing of ghrelin requires recognition of Arg/Lys residues in the sequence, an activity likely performed by gingipains. Interestingly, the maturation of ghrelin requires hydrolysis after basic residues, an activity eagerly performed by gingipains. Therefore, local production of ghrelin, modulated by bacteria in order to limit the host immune response, may lead to the disruption of the systemic levels of the hormone, leading in the chronic disease, like periodontitis, to the increase in caloric intake and development of obesity.

In recent years both periodontitis and obesity prevalence became important civilization-related diseases, which consume huge resources for health protection and significantly impair the patient’s comfort of life. Although the development of these diseases is regulated by many aspect, including genetic background, diet and lifestyle, until today their correlation was focused on the common risk factors analysis, not on the investigation of the common pathophysiology mechanism.

Tu sum up, presented project allows description of the possible causative link between periodontitis and obesity, leading to the development of novel therapeutic strategies (eg early dentist intervention and control of the bacterial growth). Moreover, as posttranslational modifications of ghrelin and its precursor by inflammation-related enzymes are included, proposed project may unveil details of the ghrelin regulation, processing and activity in the context of the developed inflammation.