What is periodontal disease?

It is an inflammatory disease of the gum and bone tissues in the mouth, called periodontal disease (PD). The disease starts from simple gum inflammation (gingivitis). It leads to serious disease that results in severe damage to the soft (gum) and hard (bone) tissues that support the teeth (periodontitis). Red, swollen, and bleeding gums characterize gingivitis. Periodontitis is characterized by slight, moderate, or severe bone loss (according to the stage of disease). During the disease progression, tooth mobility increases, teeth roots become exposed, and tooth loss may occur at the final disease stage. Since gingivitis affects only the soft tissue of the gums it is easy to treat with proper oral hygiene. In contrast, the treatment of periodontitis is complicated due to the bone loss around the teeth.

Moreover, periodontitis may also contribute to the development of such serious diseases as cardiovascular disease, rheumatoid arthritis, atherosclerosis, obesity, or complications in pregnancy.

How many people are suffering?

Currently, there are millions of adults in the world are affected by some form of periodontal (gum) disease. According to the World Health Organization severe periodontal disease, which may lead to tooth loss, is found in 20% of middle-aged (35-44 years) adults (WHO, 2012). This costs the community tens of billions of euros yearly in direct treatment costs.

How is periodontitis diagnosed and treated?

Disease diagnosis is based on clinical examinations, which state the degree of damage. However, these clinical examinations are very time-consuming and painful.

Currently, there are two ways of treatment for periodontitis patients: surgical and non-surgical. The non-surgical treatment involves painful deep cleaning (scaling and root planning) and is supplemented with medication (antibiotics). Medication is aimed at inhibiting the bacterial spread and reducing the size of tissue damage. However, the success rate of antibiotic treatment is only 50%. According to the National Institute of Health, the present-day medications alone are insufficient and cannot replace the surgery (NIH, USA 2013). Therefore, new markers for diagnosis and more efficient drugs are anxiously awaited.

What are the risk factors?

Risk factors for developing periodontitis are inadequate oral hygiene, cigarette smoking, diabetes, osteoporosis, genetic factors, age, and infections with some bacteria, for example: *Porphyromonas gingivalis, Tannerella forsythia, Treponema denticola* or *Fusobacterium nuclearum*.

What provokes disease development and progression?

The molecular cause of the disease progression and tissue (bone) damage is so-called chronic inflammation. Neutrophils and macrophages cause inflammation in response to bacterial infection. Inflammation is our body's natural defense mechanism against infection. Whereas neutrophils and macrophages are our body cells and are the most abundant among blood cells. Macrophages are crucial in killing pathogens, for example, *P. gingivalis*, *T. forsythia*, *T. denticola* or *F. nucleatum*.

Neutrophils and macrophages have two characteristic features. They promote inflammation and engulf pathogens to eliminate bacteria. First is the production of many lethal antibacterial weapons, like pro-inflammatory cytokines, enzymes, and free radicals able to kill pathogens at the beginning of the infection. However, these substances do not discriminate self from non-self. Unfortunately, this may damage the tissue surrounding tissues, as it has been recently reported as contributory to disease progression during SARS-CoV-2 infection. The second feature of those immune cells is the induction of anti-inflammatory responses after bacterial clearance by neutrophils at the end of the infection. This process, called efferocytosis, is essential for the induction of wound healing.

How will a new project financed by NCN help patients?

The project aims to study molecular mechanisms of the deregulation of neutrophils and macrophages in periodontal disease (during the infection with different pathogens i.e. *T. forsythia*, *F. nucleatum* and/or *P. gingivalis*). Importantly, we will use an in vitro approach that significantly reduces the requirement to involve animal work. This ingenious method allows for studying neutrophil and macrophage survival and their functions in a very precise and controlled way outside the organism. Obtained results will show, whether the inhibition of the macrophage survival and their function may help to cure periodontitis patients and most probably also other inflammatory diseases, similar to COVID-19 in the future.

Overall, we believe, that the development of new periodontitis diagnostic markers and therapies will bring prominent benefits to public health and the quality of life of patients suffering from inflammatory diseases.