What is periodontal disease (PD)?

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

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

How many people are affected?

Currently, there are millions of adults in the world suffering from 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 the middle-aged (35-44 years) adults (WHO, 2012). This costs the community tens of billions of euros yearly in direct treatment costs.

How is the disease diagnosed and treated?

Periodontitis diagnosis is nowadays 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 very painful deep cleaning (scaling and root planning) and is supplemented with medication (antibiotics). Medication is aimed to inhibit the bacterial spread and reduce 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 rather 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*.

What causes the disease development and progression?

The molecular cause of the disease progression and tissue (bone) damage is so-called chronic inflammation. Inflammation is caused by macrophages in response to the bacterial infection. Inflammation is our body's natural defense mechanism against infection. Whereas macrophages are our own body cells and they are the most abundant among blood cells. Macrophages play a crucial role in killing pathogens, for example, *P. gingivalis*.

Macrophages have two characteristic features. They promote inflammation and engulf pathogens in order 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. And 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 macrophages 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 is aimed to study molecular mechanisms of the deregulation of macrophages in the periodontal disease (during the infection with pathogen *P. gingivalis*). Importantly, we will use a novel *in vitro* approach that significantly reduces the requirement to involve animal work. This ingenious method allows studying 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 development of new periodontitis diagnostic markers and therapies will bring prominent benefits for public health and the quality of life of patients suffering from inflammatory diseases.