

Periodontitis is a chronic inflammatory disease of the oral cavity, caused, among others, by red complex bacteria, primarily *Porphyromonas gingivalis*. The first warning sign of the risk of developing periodontitis is gingivitis – the inflammation of the gum, which is manifested by its reddening, bleeding, and swelling. At this stage, the disease is easy to cure as it only affects the soft tissues of the mouth. However, if left untreated, mild gingivitis can become chronic, with worsening symptoms of inflammation. As periodontal disease (in short: PD) develops, the tooth roots become exposed, which may even lead to loss of teeth. Because of the loss of bone tissue, characteristic of periodontitis, this disease is much more difficult to cure than gingivitis and often requires medical attention.

The advanced form of chronic periodontitis affects around 14% of the global adult population, and its incidence increases with the age of patients. Every year, the treatment of PD requires significant financial resources - in Poland, the estimated direct and indirect expenditure is about PLN 20 billion per year (data for 2018). Unfortunately, despite the incidence of the disease, there is no single effective therapy that would allow the complete eradication of this disease. The treatment of periodontitis is largely based on very painful and non-specific mechanical removal of plaque and cleaning of the alveolar pockets. Antibiotic therapy is efficient only in half of the patients, and the growing resistance to antibiotics among bacteria and the high non-specificity of such treatment means that there is still a need to develop a more effective and less invasive method of therapy.

In the oral cavity, the most numerous group of cells are fibroblasts, which perform very important functions by producing collagen fibers that build gums and controlling the cells responsible for its removal from the tissue. Fibroblasts are also involved in the inflammatory response by regulating the activity of immune cells such as neutrophils and macrophages. During the infection with *P. gingivalis*, they are one of the first to alert the immune system to the presence of this pathogen and begin to release inflammatory agents. Unfortunately, the bacteria disguised as plaque are a difficult target for the immune cells. Unable to remove the pathogen, cells contribute to the development of a chronic inflammatory response, characterized by the continuous release of bactericidal agents into the extracellular space, which unfortunately begins to destroy the host's tissues.

The aim of the project is to characterize the effect of senotherapeutic agents - a new group of anti-inflammatory agents - on the inhibition of the inflammatory response from gingival fibroblasts. Senotherapeutics are a group of drugs aimed at eliminating senescent (aging) cells, which are the source of inflammatory factors. The action of senotherapeutic agents is based on their ability to regulate intracellular pathways controlling cell survival, e.g. apoptosis (programmed cell death). Moreover, senotherapeutic agents inhibit the pro-inflammatory activity of cells, which means that they have a high potential to be used in the treatment of chronic periodontitis. The implementation of the project will contribute to our understanding of the molecular mechanisms of PD, which might in the future lead to the development of a new method of periodontitis treatment, based on the reduction of inflammation.