

It is estimated that one in three people will develop neurodegenerative diseases during their lifetime, becoming the second most common cause of death worldwide. Alzheimer's disease (AD) is responsible for most cases of neurodegenerative diseases and is also the most common cause of dementia. The early stages of this disease manifest through memory loss, problems with concentration, changes in behaviour, and the progression of the disease leads to difficulties in carrying out daily activities, resulting in significant physical impairment and death in the final stages. The initial symptoms often resemble age-related dementia, making a correct diagnosis difficult. Nearly 120 years have passed since Alois Alzheimer described the first case of an affected person, but the cause of the development of the disease is still not known and available therapies are not effective. Risk factors for developing AD include older age, diabetes, obesity, cardiovascular disease and periodontitis.

In recent years, the antimicrobial properties of beta amyloid have been discovered, and its deposits, together with inflammation, are thought to be the most characteristic changes in the brains of patients. A link between this disease and infectious agents began to be explored. It turned out that bacterial DNA and virulence factors of the periodontopathogen *Porphyromonas gingivalis* (*P. gingivalis*), among others, were localised in the brain tissue of patients. These bacteria are part of the so-called red complex, which contributes to the disruption of the natural oral bacterial flora. This leads to inflammation, receding gingival pockets and bone destruction, which in advanced cases of periodontitis results in tooth loss. During tooth brushing, flossing and dental procedures, the bacteria and their virulence factors can enter the bloodstream, causing a number of systemic diseases such as cardiovascular disease, obesity, pneumonia, arthritis and the previously mentioned Alzheimer's disease. The mechanism by which *P. gingivalis* crosses the selective blood-brain barrier that protects the brain from harmful substances and pathogens is not yet known.

This project aims to investigate how the cells that build the blood-brain barrier (microvascular endothelium, pericytes and astrocytes) respond to infection by *P. gingivalis* bacteria and how the integrity of the barrier is altered. The bacteria produce a number of virulence factors, such as lipopolysaccharide, fimbriae and gingipains. Fimbriae allow bacterial cells to attach to host cells, and gingipains are enzymes that digest a number of proteins associated with both the body's inflammatory response and proteins responsible for tissue integrity. The properties of the aforementioned virulence factors suggest that *P. gingivalis* has a high potential to disrupt blood-brain barrier functionality via gingipains. The implementation of this project will allow the identification of changes occurring in blood-brain barrier cells at multiple levels as a result of infection. It may contribute to the identification of new therapeutic targets to prevent tissue destruction not only by *P. gingivalis*, but also by other Gram-negative bacteria causing meningitis.