

While some people age without pathological memory loss, others experience the age-related processes of degeneration and loss of brain neurons that are the basis for the development of dementia. The most common cause of senile dementia is Alzheimer's disease (AD). The number of patients with this disease in Poland exceeds 250 thousand, and in the world it reaches 50 million. It is predicted that by 2050 this number will increase to 130 million, and AD will become the cause of the world's greatest crisis. Currently, there are no drugs that can stop or cure this disease, only symptomatic treatment is available. The main reason for the lack of effective treatment is the complex and unclear causes of AD. In most cases, AD develops sporadically and asymptotically for many years. At the asymptomatic stage, however, there are many changes at the molecular level that may manifest as subjective cognitive decline (SCD). These changes are not detected by neuropsychological tests, but they are risk factors for the development of AD. The second group of people at increased risk of AD are carriers of a rare form of the gene encoding the apolipoprotein type E4 protein (APOE4). Some people at risk for AD will develop symptoms of dementia. Currently, however, there are no biomarkers that would allow to detect this disease at such an early stage. It is known that early detection of the AD risk is critically important for prevention and effective therapy. Previous clinical trials of new drugs for AD show that treatment in the later stages of the disease, when there has already been damage and death of neurons, has no chance of success. It has become clear that the condition for the development of AD prevention and treatment methods is the identification of early biomarkers of this disease in the pre-symptomatic stages, in people at risk. Furthermore, the discovery of biomarkers that reflect the complex mechanisms of AD in an individual and enable the selection of individualized treatments would be of greatest importance. Biomarkers present in easily accessible tissues, such as blood, that could be detected by simple and accessible methods are the most sought after.

This project addresses these challenges based on the results of several of our previous studies. We discovered and patented the AD's molecular signature in the form of a set of microRNA (miRNA) molecules. These molecules are short fragments of non-coding RNA secreted into the blood, which perform important regulatory functions in the body's cells. We found that the miRNAs we identified are involved in numerous AD pathological processes and may be their markers. In addition, we have included other miRNAs reproducibly identified in the last 10 years as potential markers of AD in the blood. This project is based on our pioneering hypothesis that the molecular signature of miRNAs in the blood, discovered in the last decade, reflects the complex pathomechanisms of AD, and therefore that miRNAs are more suitable for the early detection of this multifactorial disease than any other existing test.

The aim of this project will be to investigate whether the miRNAs selected by us are biomarkers not only of the later stages of AD, but also of the pre-symptomatic stage in people at risk of AD (people with SCD, APOE4 carriers). We will check whether the selected set of miRNA molecules can indicate which people from the risk groups develop asymptomatic AD. We will also check whether any miRNAs of our kit are changed differently in women and men and in different stages of AD. We will also check whether there are miRNAs in the kit that predict the development of not only AD, but also other types of dementia. In the research, we will use molecular methods optimized by us and machine learning methods, which are currently one of the most outstanding fields of artificial intelligence, with many applications, including in the diagnosis of diseases.

A future early-stage AD test based on the use of blood miRNAs would be more clinically available than any existing AD tests, such as cerebrospinal fluid tests or brain imaging techniques. In addition, this test, reflecting the multifactorial nature of AD, would bring a new quality to the diagnosis. The project therefore represents research that could revolutionize the future diagnosis of AD and enable early prevention or individualized therapies.