

## **Evaluation of circulating miRNA expression in patients with selected primary headaches**

Nearly everyone has heard of migraine and about 15% of the population experiences it themselves. Migraine is more than just a strong headache. It is often accompanied by extreme sensitivity to light and sound, nausea and vomiting and its symptoms may last as long as seventy-two hours. Although a common and well-known condition with available treatment, it still interferes with the professional duties, social life and leisure activities of people living with it. According to WHO Global Burden of Disease Study migraine belongs to conditions with most Years Lived with Disability.

Compared to migraine, cluster headache is significantly less common. This is likely the reason why, although its symptoms are characteristic, it often remains unrecognized for many years. Sufferers visit various physicians, such as ear nose and throat specialists, dentists or ophthalmologists and some of them turn to alternative medicine, before, often after many years, the right diagnosis is made. Sometimes they undergo unnecessary invasive procedures, such as sinus or nasal septum surgeries or tooth extractions. However, the most common misdiagnosis of cluster headache is migraine.

Today, primary headaches, which are the ones occurring without another underlying disease, are diagnosed based on clinical symptoms, most commonly described by the patient during an interview, much less frequently observed by the doctor. Although diagnostic criteria of individual pain syndromes are precisely defined, this way of making a diagnosis leaves room for communication errors. This applies especially to situations, when the communication with the patient is difficult, for example due to a language barrier or dementia, or in the case of little experience of the examiner. Considering this, an objective, measurable biomarker could facilitate proper diagnosis and differentiation between headache syndromes.

One of the proposed potential markers of migraine are circulating microRNAs (miRNAs), which are short particles of ribonucleic acid, taking part in the regulation of gene expression. Until recently, it was believed that they could only be found in cells. However, they have been detected in blood, cerebrospinal fluid, urine, milk and seminal fluid. Although their biological role is yet to be determined, thanks to their robustness and the possibility to obtain them using minimally invasive procedures, circulating miRNAs gain growing interest as biomarkers of pathological states. Studies have shown that the profile of circulating miRNAs differs from healthy population, among others, in patients with various types of cancer, neurodegenerative conditions, like Alzheimer's or Parkinson's diseases, or pain disorders, for instance complex regional pain syndrome.

Previous studies on their role in migraine have shown that also in these patients the levels of individual circulating miRNAs differ from that detected in healthy control group. Limited numbers of people examined, as well as differences in used biological material and analyzed miRNAs do not allow the unambiguous identification of those molecules that could act as biomarkers of this condition. Additionally, differences between the results of people suffering from episodic and chronic migraine have not been studied, and the results of research on other potential markers give grounds to believe that they may occur. So far, similar studies have not been conducted in patients with other headache syndromes, such as cluster headache, therefore it is not known whether differences in the levels of individual miRNAs could be useful in distinguishing these conditions.

In our project, we plan to compare the profile of circulating miRNAs of patients suffering from episodic and chronic migraine or cluster headache with the profile of healthy people matched in terms of age and sex. By including patients with both migraine and cluster headache in the study, we will be able to determine whether this profile is characteristic of a specific type of headache and whether its assessment could potentially distinguish between these diseases. For the first time, we will have a chance to compare miRNA profiles of patients with an episodic and chronic form of migraine, which may provide new information about the process of pain chronification. Project results will provide a basis for further research into the possible use of circulating miRNAs not only as diagnostic, but also as therapeutic biomarkers.