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microRNA and response to anti-VEGF therapy of neovascular age-related macular degeneration in a Russian cohort: experience of use as a tool for personalized medicine

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The leading cause of vision loss in older adults is age-related macular degeneration (AMD). AMD is a multifactorial neurodegenerative disease of the retina, the nature of which depends on many interacting factors: genetic, environmental, and epigenetic, including changes in microRNA expression patterns. MicroRNAs are small non-coding regulatory RNA molecules that modulate the expression of target genes by blocking translation through complementary binding of messenger RNAs. The freeze-thaw stability of microRNAs in plasma/serum/urine and the availability of quantitative detection methods expand the possibilities of their use as biomarkers, as well as potential mediators of physiological and pathological processes. Assessing the circulating pool of miRNAs in various biological fluids, such as blood plasma, is considered a promising approach to diagnosing AMD and assessing the effectiveness of therapy, which may contribute to early detection of the disease and monitoring of AMD progression. We conducted a study aimed at evaluating the microRNA profiles of patients divided into groups: patients with neovascular AMD who demonstrated a good response to anti-VEGF therapy, patients with a poor response, and a control group without fundus pathology. To assess miRNA expression in blood plasma, a highly sensitive profiling method on PCR panels with preadsorbed LNA primers (miRCURY, Qiagen) covering 179 miRNAs was used. The analysis showed significant variability in miRNA expression, with clustering of AMD and control groups observed. Significant changes in the level of 12 miRNAs were established. In the group of patients with a poor response in plasma, a significant increase in miR-27 and miR-23 microRNA levels was observed. It is known that these miRNAs are expressed by endothelial cells and belong to the miR-23~27~24 gene cluster responsible for the regulation of angiogenesis and the development of retinal vessels. Using bioinformatics approaches, target genes of differentially presented miRNAs and pathways regulated by them, potentially involved in the pathogenesis of neovascular AMD, have been identified. A high level of miR-27a in patients with neovascular AMD was verified by quantitative PCR with Taqman samples using an independent expanded sample. Moreover, according to optical coherent tomography data, in patients with a weak decrease less than 10 % in the CRT after 3 loading doses of the anti-VEGF drug the level of miR-27a was significantly increased compared to patients with a decrease in CRT by more than 25 % ($p = 0.039$), which confirms the potential role of this miRNA as a marker of poor response to antiangiogenic therapy.

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