CLONAL HEMATOPOIESIS AND ITS ROLE IN THE DEVELOPMENT OF CARDIOVASCULAR DISEASES

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Clonal hematopoiesis (CH) is the increase in somatic clones carrying mutations in hematopoietic stem cells. This biological condition can lead to cancer and is implicated in the development of atherosclerosis and cardiovascular diseases. CH of indeterminate potential (CHIP) refers to somatic mutations in genes that are associated with the development of Coronary heart disease (CHD) and leukemia.

Now, with next-generation sequencing, we can detect mutations even if they are present in only a small number of cells in the tissue sample being studied. Consequently, numerous studies have shown that mutations in the DNMT3A, TET2, ASXL1, and JAK2 genes found in the blood are associated with coronary heart disease.

The purpose of our study is to detect a genetic variant of genes in Kazakh patients with atherosclerosis, which will further allow us to study the role of CHIP in increasing the risk of developing coronary microvascular dysfunction and CHD.

We perform high-throughput whole-exome sequencing in patients with atherosclerosis.

The object of the study is samples delivered from the clinic "National Scientific Cardiac Surgery Center" in Astana. The study is carried out in accordance with the principles of the Declaration of Helsinki of the World Medical Association.

Genomic DNA extraction was performed on 245 samples using the Illustra Blood Kit (Cytiva, USA). Qualitative and quantitative assessment of the extracted genomic DNA was conducted using the NanoDrop 2000 (Thermo Scientific) and Qubit 2.0 (Thermo Fisher Scientific). Subsequently, DNA library preparation was carried out using the Illumina DNA Prep with Exome 2.5 Enrichment kit. Quality control of the resulting DNA libraries was conducted on a 2100 Bioanalyzer system using the Agilent DNA 1000 Kit and High Sensitivity DNA kit (Agilent Technologies). Following assessment of the DNA library concentration on Qubit 2.0, they were loaded onto the high-performance sequencer NovaSeq 6000 (Illumina, USA) following the manufacturer's protocol.

We conducted human whole-exome sequencing on 245 samples to identify somatic clones in the peripheral blood of patients with atherosclerosis. Patients were divided into three groups – low risk, middle, and high risk of atherosclerotic complications. Bioinformatic analysis of sequence data were performed. We created list of genes associated with CH to deep analysis and to interpreter the data in patient groups. Subsequently, DNA extraction from the remaining samples is performed, followed by sequencing on the NovaSeq 6000 platform. Analysis of the resulting sequenced data is currently underway.

Further research and monitoring of CHIP will enable us to understand the mechanisms underlying the development of cardiovascular diseases and to devise a comprehensive management plan for patients with this pathology.

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