GENETIC VARIANTS, METABOLOME, AND GUT MICROBIOME BIOMARKERS FOR OBESITY AND AGING IN RANDOMLY SELECTED KAZAKH INDIVIDUALS

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Objective: Metabolic syndrome (MS) is a cluster of inter-related and heritable metabolic traits, which collectively impart unsurpassed risk for atherosclerotic cardiovascular disease and type 2diabetes. Considerable work has been done to understand the underlying disease mechanisms by elucidating its genetic etiology. Genome, Metabolome variations and gut microbiome can predict disease risk and diagnosis and help to understand molecular pathophysiology. We aimed toassess plasma metabolom differences and gut microbiome as well as genetic variants among Kazakh population to identify and characterize the genetic, metabolic profiles and host-gut microbiota interactions.

Methods: Kazakhs were recruited into study after signing of informed consent in Astana, Kazakhstan. Ultrahigh Performance Liquid Chromatography-Tandem Mass Spectroscopy (UPLC-MS/MS) (Metabolon, USA) and NGS16S rRNA gene-sequence-based methods were used. Bioinformatic and statistical analyses were performed.

Results: Subjects were stratified by age (young <45y, old ≥45y), gender and BMI. 853 different biochemical indicators of the main pathways for the metabolism were identified in plasma. Results demonstrate alterations in various metabolic pathways in older participants compared to younger subjects. Metabolic differences included changes in metabolites associated with the metabolism of fatty acids, steroidogenesis, secondary carnitine metabolism, inflammation and oxidative stress. Microbiomes of older persons are characterized by a high level of microorganisms involved in the processing of plant substrates, butyrate-producing bacteria and also has higher values of opportunistic microorganisms, representatives of the Tenericutes family. The biodiversity index of the microbiome of older persons is reduced in comparison with the biodiversity index in younger participants. This may indicate the influence on the microbiome characteristics of such factors as genotype, nutrition, lifestyle.Genetic risk factors associated with the obesity and hypertension were identified.

Conclusions: Understanding plasma metabolome and gut microbiome is essential to the development of future personalized strategies of healthcare. Genome-wide association studies (GWAS) have been widely utilized albeit with modest success in identifying variants that are associated with more than two metabolic traits. Further studies with detailed analysis are needed to clarify host-gut genetic and metbolome interactions.

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