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Revealing the molecular basis of interactions of COVID-19 with hyperglycemia and diabetic complications based on the bioinformatics analysis of the gene networks

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Motivation and Aim: People with diabetes are more likely to have severe COVID-19 compared to general population. Moreover, diabetes and COVID-19 demonstrate a certain parallelism in the mechanisms and organ damage [1]. We applied bioinformatics analysis of associative molecular networks to identify key molecules and pathophysiological processes that determine SARS-CoV-2-induced disorders in patients with diabetes.

Methods: The text-mining based approaches of ANDSystem [2, 3] were used in this study for reconstruction and analysis of gene networks. The gene network associated with hyperglycemia was reconstructed in the study [4]. The list of 332 SARS-CoV-2-targeted proteins was extracted from the publication [5]. The Gene Ontology enrichment analysis was performed by DAVID online tool [6]. The networks of vascular diabetic complications were obtained from works [4, 7].

Results: Firstly, we have reconstructed and matched the network associated with hyperglycemia and the network of SARS-CoV-2-targeted proteins. These networks included 430/332 genes/proteins and 46855/1664 interactions respectively (Figure).

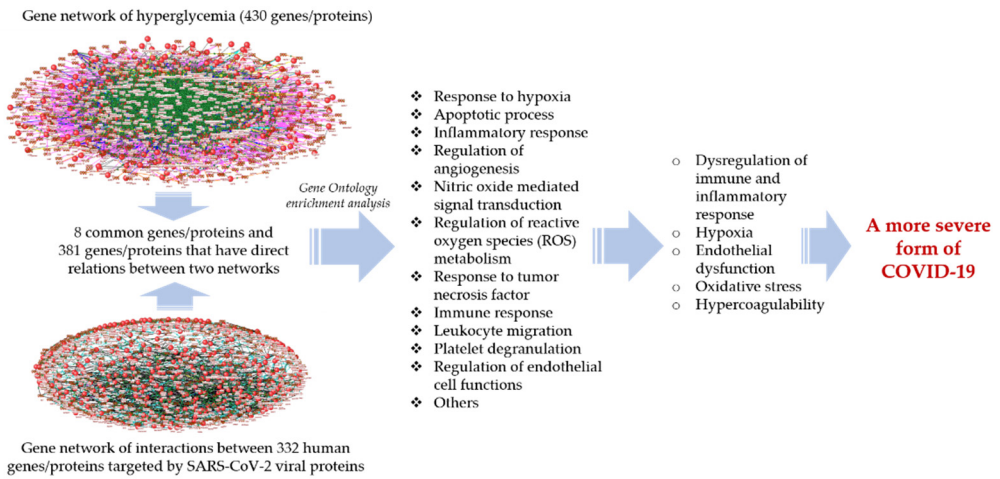

Fig. 1. Interconnections between the hyperglycemia gene network and the network of SARS-CoV-2-targeted proteins are involved in a number of biological processes which disruption leads to some pathological states that contribute to the development of a more severe form of COVID-19 in patients with diabetes

Eight hyperglycemia-related genes/proteins (DNMT1, FBN1, GDF15, GPX1, HMOX1, IDE, PLAT, and RHOA) were also targeted by SARS-CoV-2. Besides, 381 molecules were directly connected between two networks by protein-protein or regulatory connections. These molecules, according to Gene Ontology enrichment analysis, are involved in response to hypoxia, reactive oxygen species metabolism, immune and inflammatory response, regulation of angiogenesis, platelet degranulation, and other processes (Figure).

A number of genes/proteins targeted by SARS-CoV-2 (BRD2, COMT, DNMT1, ERP44, F2RL1, GDF15, GPX1, HDAC2, HMOX1, HYOU1, IDE, LOX, NUTF2, PCNT, PLAT, RAB10, RHOA, SCARB1, and SELENOS) were found in the networks of insulin resistance and vascular diabetic complications.

Conclusions: The results expand the understanding of the molecular basis of diabetes and COVID-19 comorbidity.

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