Computational studies on Gene Ontology for Molecular functions, Cellular component and Biological process of SARS-CoV-2 targeted proteins

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Short Report

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Abstract

World is facing pandemic COVID-19 caused by SARS-CoV-2.Researchers are working to identify potential cure and treatment for COVID-19. Many Repurposed drugs been proposed to treat the infection with good success rate in some cases. But still there is an urgency to discover potential cure and treatment. In order to discover potential cure we should understand the Gene Ontology of targeted proteins of SARS-CoV-2 for their Molecular functions, cellular component and Biological process. Spike glycoproteins, Main protease (Mpro), Papain like protease (PLpro) are three main proteins that aid viral host cell entry and its replication causing pathogenesis. Using MetaGO an algorithm an algorithm for predicting Gene Ontology (GO) of proteins the Molecular functions, Cellular component and Biological process of SARS-CoV-2 proteins studied. MetaGO analysis had predicted Spike protein gene ontology functions include host cell surface binding, receptor binding, host cell surface receptor binding, structural molecule activity, carbohydrate binding. Main Protease (Mpro) and Papain like protease (PLpro) gene ontology functions predicted hydrolase activity, RNA-directed RNA polymerase activity, ubiquitinyl hydrolase activity, Lys48-specific deubiquitinase activity, mRNA (nucleoside-2'-O-)-methyltransferase activity, mRNA (guanine-N7-)-methyltransferase activity, double-stranded RNA binding, 3'-5'-exoribonuclease activity, helicase activity, single-stranded RNA binding, cysteine-type endopeptidase activity, omega peptidase activity, zinc ion binding, thiol-dependent ubiquitinyl hydrolase activity, ATP binding, endonuclease activity among which PLpro had shown inhibition of ISG15 activity in additional. Inhibition of ISG15 indicates down regulation of interferon production particularly Interferon Type 1. PYCR1 (Pyrroline-5-carboxylate reductase 1) which protects the cells from mitochondrial damage due to oxidative stress shown to be inhibited by Spike protein hydrolase like activity and leading to cell death.PYCR1 can be a diagnostic tool to detect novel coronavirus infection. Viral proteins also use cellular Ubiquitinyl enzymes for its replication and survival in host cell. Thus through gene ontology studies we propose use of Interferon type 1 therapy against COVID-19 caused by SARS-CoV-2.

Background

Presently world is facing pandemic COVID–19 caused by SARS-CoV–2 and took more than 70,000 lives as per existing records from all over the globe. There is an urgency to understand the pathogenesis of the virus and to discover proper cure and treatment. Large number of infected people and their clinical studies had reported so far had shown severe Respiratory syndrome, diarrhoea, fever and other inflammations. Genome mining analysis had shown SARS-CoV–2 is stable even at temperature above 45^0C (thermally stable) and can circulate in air more than an hour. Some had shown SARS-CoV–2 virus had already mutated and might have two to four varieties circulating among patients as Coronavirus are known for their mutation. Structural analysis of SARS-CoV–2 had Lipid wrapped envelop with glycoproteins like Spike, hemagglutinin-esterases with SS-RNA and proteolytic enzymes like papain-like protease (PLpro) and Main protease (Mpro). Structural and functional analysis can be obtained by gene

ontology of above mentioned SARS-CoV–2 proteins through which it is easy to discover proper cure or treatment for COVID–19.

Methods

Confirmatory structures and their sequences were obtained from RCSB database with PDB ID: 6VSB for spike protein, 6W9C for papain like protease and 6LU7 for Main protease (Mpro). MetaGO is an algorithm for predicting Gene Ontology (GO) of proteins [1]. It uses three frameworks to detect functional homologs through local and global structure alignments through sequence to sequence profile comparison and partner-homology base protein-protein interaction mapping thus provides functional insights by combination of the three pipelines through logistic regression. The protein sequences are submitted to MetaGO either in FASTA format or PDB format for Gene Ontology.

Results

MetaGO analysis of protein sequences for spike, Main protease (Mpro) and Papain like protease (PLpro) had predicted Gene ontology for Molecular function, Biological process and Cellular components as shown in tables 1,2,3,4,5,6,7,8 and 9. Main Protease (Mpro) and Papain like protease (PLpro) gene ontology functions predicted hydrolase activity, RNA-directed RNA polymerase activity, ubiquitinyl hydrolase activity, Lys48-specific deubiquitinase activity, mRNA (nucleoside–2’-O-)-methyltransferase activity, mRNA (guanine-N7-)-methyltransferase activity, double-stranded RNA binding, 3’–5’-exoribonuclease activity, helicase activity, single-stranded RNA binding, cysteine-type endopeptidase activity, omega peptidase activity, zinc ion binding, thiol-dependent ubiquitinyl hydrolase activity, ATP binding, endonuclease activity among which PLpro had shown inhibition of ISG15 activity in additional. Spike protein gene ontology functions include host cell surface binding, receptor binding, host cell surface receptor binding, structural molecule activity, carbohydrate binding. Papain like protease Molecular function showing inhibition of ISG15 activity indicates lowering of immune function by inhibiting interferon type1. Based on Molecular functions, Biological predictions and Cellular component gene ontology report it will be an easy aid for researchers to design treatment protocol against COVID–19. From the PLpro inhibition activity against ISG15 indicating down regulation of interferon Type 1 production in host body. Treatment with Interferon Type 1 (Interferon α/β) may support in treatment protocol against COVID–19 which can be proven through proper clinical studies.

Declarations

Competing interests: The authors declare no competing interests.

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Tables

Due to technical limitations, Tables 1-9 are provided in the Supplementary Files section.

Supplementary Files

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- Tables.docx
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