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A new mechanism of Corona virus pathogenesis: Corona virus RNA Topoisomerase (Nsp2) and rRNA Methyltransferases (Nsp9/10/13/14/16) as therapeutic targets

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Corona virus infected ~100 million people with confirmed >900000 deaths worldwide whereas lockdown has reduced GDP 2-20% of many countries with 20 million jobless. So far no proper medicine was discovered and worldwide efforts for vaccine development against S-protein at the 3rd phase of clinical trial. We found that Nsp2 non-structural protein derived from polyprotein of coronavirus was not known and disclosed as RNA topoisomerase by homology search with Vibrio haemolytica DNA topoisomerase I & IV as well DNA primase and bi-subunit DNA topoisomerase IB of Trypanosoma brucei and DNA gyrase of Escherichia coli. Further, we found Nsp16 was a 2'-O-Ribose Uridine Methyltransferase and Nsp13 was a 2'-O-Ribose Guanosine Capping Methyltransferase previously implicated as RNA helicase. Search with 200 RNA/DNA binding-modifying proteins confirmed Nsp13 protein has scattered homology to ribosomal L6 and L9 proteins and Nsp2 protein to L1 protein and Nsp15 protein to S1/S22 ribosomal proteins. Further, Nsp13 has some homology with Cfr 23S rRNA methyltransferase and RNaseT whereas Nsp15 to Dcm DNA methyltransferase and Nsp14 to Cfr 23S rRNA methyltransferase. Further, Nsp8, Nsp9 and Nsp10 have some similarities to Rlm-types methyltransferases of E. coli and also some different ribosomal proteins similarities. These bioinformatics data suggested that Nsp2, Nsp8, Nsp9, Nsp10, Nsp13, Nsp14 and Nsp16 non-structural proteins may be recruited easily to mitoribosome making chimera ribosome to methylate the 21S rRNA of human mitochondria or change its topology favouring viral protein synthesis and inhibiting host protein synthesis. Such change in host protein synthesis (CoxI/II) in the mitochondria may cause a inhibition in oxidative phosphorylation and ATP synthesis causing blood clotting, breath trouble, coma and heart failure as seen in many corona-infected patients. Thus, targeting those viral mRNA and proteins with drugs, antisense, ribozyme and CRISPR-Cas6 may save life. So far, only Nsp12 (RNA-dependent RNA polymerase) and Nsp3 (C3 protease) proteins were targeted for drug design against corona virus.

Biography:

A molecular biologist experienced in bacteriology, protein purification, mammalian cell culture, plant tissue culture, retrovirology, gene therapy, gene transcription and drug discovery.

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