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Short Communication

Molecular Targets and Biotechnological Exploration on Corona-Virus and Multi-Drug Resistant Bacteria

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Invisible SARS-CoV-2 27kb single (+)-stranded RNA virus (120nm) has crossed limit by killing 3 millions and affecting 600 millions [1]. Severe COVID-19 is more common in adults aged ~70 years and older and in individuals with comorbidities such as hypertension, diabetes, cardiovascular disease, and chronic respiratory disease [2]. Indian Government as well as other G-20 nations declared war against Corona virus. Coronavirus has structural proteins (S, M, N, E) and two large polyproteins which degraded into sixteen non-structural proteins (nsp1-16) [3]. No new targeted drug was discovered and vaccine is only new hope. Presently, at least ten vaccine candidates are in stage-III clinical trials on 20 - 40 thousand human worldwide [4-8]. It is expected that India should be starting vaccination in the middle of 2021 with a cost of few hundred to few thousand per dose. Vaccine usually is a protein or synthetic peptides from Corona virus that can elicits humoral antibody (IgG) as well as T-cell mediated ability to destroy virus.

Attenuated or killed Corona virus (Covaxin, Bharat Biotech) also used like Pox vaccination. As genetic information in cells processed from DNA to RNA to protein, scientists have exploited DNA vaccine as well as RNA vaccine for the protection of Corona virus. Indian Serum Institute uses protein as well as killed virus whereas Russia uses mRNA vaccine (Sputnik V) and England (Oxford + Astra-Zeneca) uses S protein DNA vaccine using adenovirus vector (Ad5 or Ad26) [8]. USA (Moderna/Pfizer) and Germany's BioNTech uses mRNA vaccine. The most people use spike protein (S -protein) which is the receptor protein of coronavirus that bind to ACE-2 receptor of lung cells of human and animal. American pharmaceutical giant Pfizer and its German partner BioNTech submitted an application to the FDA for emergency use authorisation of its vaccine. Oxford and AstraZeneca expect to produce up to three billion doses of the vaccine in 2021. Moderna expects to have 20 million doses ready by the end of the year and says it remains on track to deliver at least 500 million doses per year. Questions have also been raised over the vaccine's storage, which requires ultra-cold freezers set at minus 20-70 degrees Celsius. It was reported that efficacy of vaccination vary from 60 to 95% where Adeno-virus mediated delivery appears more successful.

We predicted other coronavirus proteins like proposed RNA topoisomerase (nsp2) and rRNA methyltransferases (nsp13, nsp16) may be good protein or peptide vaccine [9,10]. RNA-dependent RNA polymerase (nsp12) which is target for drug remdesivir as well as proteases (nsp3 and nsp5) may be also candidates for drug and vaccine candidate [11].

We also observed that MDR infections is a comorbidity in coronavirus infection [12-16]. *Klebsiella pneumonia* contains many MDR conjugative plasmids and resistant to 100 antibiotics due to presence of mdr genes like blaNDM-1, blaCTX-M, blaOXA, cat, strA/B, aph, aacC1, aacA1, sul1/2/3, aad, arr etc. as well as drug efflux genes like tetA/B, acrAB, mexAB/CD/EF, macAB etc [12]. One alternate approach is phyto-drug from Indian medicinal plants as described in Sanskrit books Charka Samhita and Atharva-Veda and Chinese books. We showed bark and root of *Cassia fistula* and *Suregada multiflora* chemicals (CU1/3, NU2/3) very efficiently inhibited multi-drug resistant bacteria isolated from Ganga River water or animal and human [17]. Thus, fungal fermentation for antibiotics may be ended and cultivation as well as purification of phyto-chemicals will be started highly to control superbugs infections. Thus, a new biotechnological arena was established for both Coronavirus and MDR-bacteria therapeutics discovery.

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