QUICK REVIEW ON THE MERS-COV, SARS-COV AND SARS-COV-2 CORONAVIRUS

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INTRODUCTION

The human coronaviruses was first identified in mid 1960s. Coronavirus are subgrouped in alpha, beta, gamma & delta. Severe Acute Respiratory SyndromeCoronavirus (SARS-CoV and SARS-CoV-2) & Middle East Respiratory Syndrome Coronavirus(MERS-CoV) are included in Beta coronaviruses (Sharifi-Mood 2015; Ksiazek etal., 2003, Cho et al., 2016., Kim et al., 2015). Coronaviruses are viruses thatbelong to the subfamily of Coronavirinae in the family of Coronaviridae, causesthe common cold and severe acute respiratory syndrome; they are well known tocause disease in humans and animals including himalayan palm civets, raccoon,monkeys, dogs, cats, dogs, and rodents. MERS-CoV is genetically distinct fromthe SARS-CoV and SARS-CoV-2, which has emerged as a pandemic in the last decade and appearsto behave differently (Baseler et al., 2015; Yang et al., 2015). Incidence of Humancoronaviruses infection among infants is highest during the winter and earlyspring seasons.Middle East Respiratory Syndrome (MERS) is a syndrome affecting upperrespiratory system and is caused by Middle East Respiratory SyndromeCoronavirus (MERS-CoV). MERS cases high fever, chills, chest pain, bodyaches, cough, breathing problem, sore throat, diarrhoea, renal failure, pneumonia,nausea/vomiting and running nose. First case of MERS to human was reported inyear 2012 in Saudi Arabia. After 2012 MERS-CoV infection has been reportedfrom 27 countries only within 4 years (WHO report: 2016). Till present threeMERS outbreaks have taken place in Saudi Arabia (2013, 2014) and in SouthKorea (2015) (Assiri et al., 2013; Oboho et al., 2015; Park et al., 2015). Outbreakreported in South Korea was reported to have fatality rate as high as 40%, and italso involved spreading of MERS while hospital-to-hospital transit of patients.High attack rate and easy spreading means has put MERS disease at risk of anepidemic (Kim et al., 2015; Ki., 2015; WHO Emergencies preparedness,response, 2015). Till date no specific vaccine is available against MERS. There isan urgent need for specific and safe MERS vaccine keeping in mind the steepincrease of MERS cases and it's high mortality rate. As far now the pathogenesisof MERS-CoV is largely unknown. Hence, an immunoinformatics approach tothoroughly study and screen potential immunogenic proteins from availableproteome sequence data of MERS-CoV is very essential for vaccine development.SARS started off in the Guangdong Province in southern China in themonth of November 2002. Eventually it reached Hong Kong, from where itrapidly spread around the world, infecting people in 37 countries (Hsieh et al.,2015., Kong et al., 2015). Severe acute respiratory syndrome coronavirus (SARSCoV)causes a severe form of upper respiratory track disorder called the Severeacute respiratory syndrome (SARS). The SARS infection is highly contagious andis prominently characterized by breathing difficulties, high fever, dry cough, andpneumonia. SARS is endemic in southern China. In the year 2003, the SARSoutbreak in south China caused 8098 people sick and 774 dead. Eventually, SARShas now reported to spread around the world, infecting people in 37 countries(Zhong et al, 2003; Booth et al., 2003; Leung et al., 2003; CDC report; 2018).Even though there is an urgent need to develop a specific SARS vaccine, till datethere is no specific and safe vaccine against SARS. Pathogenesis mechanism ofSARS-CoV and SARS-CoV-2 being still largely unknown the immunoinformatics approach todesign and develop an epitope-based specific vaccine against SARS would be anessential step forward.

The MERS-CoV, SARS-CoV and SARS-CoV-2 Coronavirus

The proteome of MERS-CoV consists of several vaccine candidate proteins aswell as drug target proteins. These proteins are mostly involved in infection andpathogenesis process of the MERS-CoV to human host cells. The Spike (S)glycoprotein, in particular, its receptor-binding domain (RBD) is involved in thevirus-host cell interaction (Wang et al., 2015). Envelope (E) protein plays anessential role in the host cell recognition (Xie et al., 2017). Nucleocapsid (N)protein is involved in the RNA binding, during ribonucleocapsid formation byMERS-CoV (Wang et al., 2015). Membrane (M) protein has important roleinvolving its interferon (IFN)-antagonizing properties and reducing IFN levels ininfected patients (Lui

et al., 2016). Open reading frame (ORF) proteins playcritical roles in viral infection and the pathogenesis. Mutational studies on ORFs(ORF3, -4a, -4b, and -5) proteins has indicated that ORFs have major implicationsin viral infection causing disruption of host cell, disordered interferon (IFN)pathway, and abrupt inflammation (Menachery et al., 2017). Proteins ORF1a(4P16) and ORF1ab (4WUR) are papain-like proteases (PL(pro)) and are involvedin viral infection, hence these proteins are potential target for the development ofantiviral drugs (Lei et al., 2014). The papain-like proteases facilitate infection bytheir proteolytic, deubiquitinating activity, and deISGylating activity suppressingthe innate immune response from the host cell. The ORF1a (4RSP) protein is aprotease (3CLpro) and it provides proteolytic activity during viral infection andreplication (Tomar et al., 2015; Lei et al., 2016). Protein ORF 1ab (5WWP) is ahelicase protein of MERS-CoV, this protein is one of the most conserved proteinsamongst nidoviruses. Protein ORF8b is a highly conserved and while infection itis involved in inducing various immune response (Lu et al., 2015).All the above proteins of MERS-CoV are critically involved inpathogenesis of the virus to the human cells. Hence, are chosen to screen outpotential epitopes to design Multi-Epitope Vaccines (MEVs) and Multi-Patch vaccine against MERS-Cov, SARS-CoV and SARS-CoV-2. Thedesigned and proposed MEVs in this study are composed of Cytotoxic Tlymphocyte and Helper T lymphocyte (CTL and HTL) epitopes. Both the CTLand HTL MEVs also contain overlapping regions of linear B cell epitopes. Boththe MEVs were designed to have human β Defensin 2 and human β Defensin 3 asadjuvants for the purpose to enhance the immunogenic response (Duits et al., 2003; Wilson et al.,2013).The proteome of SARS-CoV and SARS-CoV-2 consists of several important drug target andvaccine candidate proteins. the present study covers screening of potentialepitopes from eleven different SARS-CoV and SARS-CoV-2 proteins. All the chosen proteins arecritically involved in virus-host interaction and pathogenesis. The Spike (S)protein of SARS-CoV and SARS-CoV-2 is involved in membrane fusion and viral entry into thehuman host cell (Du, et al., 2009; Liao, et al., 2015). The Envelope (E) protein isinvolved in anchoring and hence plays a determining role in virus-human host cellinteraction and viral pathogenesis (Jimenez-Guardeño, et al., 2014). Themembrane (M) protein is important for assembly and budding of viral particlesand hence is a crucial protein for viral pathogenesis (Voß, et al., 2009). Thenucleocapsid (N) protein is involved in packaging of the viral genome into ahelical ribonucleocapsid, hence are involved in viral self-assembly andpathogenesis (Wei, et al., 2012; Chang, et al., 2014). The ORF (Open ReadingFrame) 3a protein plays an important role in viral replication and hence is apotential target for drug and vaccine design (Lu, et al.,2009;Åkerström, et al., 2007; Zhong, et al., 2006). The ORF 3b protein is involved in the upregulation oftranscriptional activity during pathogenesis and hence 3b protein is a potentialdrug and vaccine design target (Åkerström, et al., 2007; Varshney, et al., 2012).The ORF 7a protein is involved in the viral replication cycle (Åkerström, et al., 2007; Vasilenko, et al., 2010). The ORF 7b protein is involved in virusreplication as well as it enhances virulence (Pfefferle, et al.,2009; DeDiego, et al., 2008). The ORF 8a protein enhances viral replication as well as it also induceshost cell apoptosis (Chen, et al., 2007). The ORF 8b protein plays important rolein viral replication and it also induces DNA synthesis (Law, et al., 2006). TheORF 9b protein enhances pathogenesis by suppressing innate immunity (Shi, etal., 2014). All the above-discussed eleven proteins of SARS-CoV and SARS-CoV-2 play importantrole in either viral proliferation or human host cell pathogenesis hence arepotential targets for drug and vaccine design and were chosen for further study.

CONCLUSION

In the present study, we conclude that a more specific and targeted strategy to design vaccine against Coronaviruses is required. The Multi-Patch design vaccineagainst MERS-CoV, SARS-CoV and SARS-CoV-2 have been validated for stable complex formation with ectodomain of TLR3. Hence the novel Multi-Patch Vaccine design by utilizing antigenic patches (Ag-Patches) could be a potential candidate to combat MERS-CoV, SARS-CoV and SARS-CoV-2, with higher effectiveness, higher specificity and larger human population coverage.

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