Understanding SARS-CoV-2
A closer look into its genome

A team of BARJ scientists from the Bangladesh Jute Research Institute, Dhaka, Bangladesh have conducted significant research on SARS-CoV-2, the virus responsible for causing COVID-19. In a recent research project, BARJ researchers collected samples from positive coronavirus patients and conducted a comparative study to analyse differential host responses in various SARS-CoV-2 infection systems. In another project, the research team predicted potential intermediate hosts of the COVID-19 virus that can spread this infection in the southern region of Asia.

The coronavirus pandemic has spread across the globe and killed more than three million individuals. It is caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), and is thought to have originated in bats and spread to humans through intermediate hosts. The number of COVID-19 patients is increasing at an alarming rate across many countries. Scientists around the world are working tirelessly to understand the mechanism of the virus and find better therapeutic interventions to control the rate of infection.

DIFFERENT TRANSCRIPTIONAL HOST RESPONSES IN COVID-19 PATIENTS

Using the latest sequencing technologies, BARJ researchers from the Bangladesh Jute Research Institute designed a study to sequence the genome of SARS-CoV-2 from Bangladeshi patients. They began with collecting nasopharyngeal (upper part of the pharynx, connects nasal cavity above the soft palate) swab samples of COVID-19 positive patients from the Chattogram region with support from the Chattogram Veterinary and Animal Sciences University. Their aim was to profile the COVID-19 patient transcriptome (the sum of all the messenger RNAs molecules expressed by the genes in an organism) from nasopharyngeal swabs and the genomic features of the virus isolated from each host. They compared differential host responses in several SARS-CoV-2 infection systems.

One of a kind, this study from South Asia reports genome variations observed in the four SARS-CoV-2 isolates. The researchers investigate the variations in host transcriptional responses in various COVID-19 infection models and potential consequences of these changes. The mapped reads were assembled de novo (a method for constructing genomes from a number of DNA fragments). The team applied the “Variation Identification” tool on the China National Center for Bioinformation’s “2019 Novel Coronavirus Resource (2019nCoVR)” portal to identify the variations in their sequenced SARS-CoV-2 genome. They then utilised the same portal’s “Variation Annotation” method to annotate the variations of the isolated SARS-CoV isolates. The Ensemble Variant Effect Predictor (VEP) tool was applied to further characterise the impacts of the variations.

All of the reported isolates had unique and rare missense mutations in the 3C-like protease. According to the functional enrichment analyses, innate immunity, interferon, and cytokine activation were involved in the host-induced responses. Surprisingly, these patients show no activation of apoptosis, phagosome, antigen presentation, or hypoxia (deficiency of oxygen) response. In the lungs, immune and cytokine signalling genes including CCL4, TNFA, IL6, IL1A, CCL2, CXCL2, IFN and CCR1 were found to be up-regulated. There was a lack of angiogenin 1 converting enzyme -2 (ACE2) overexpression in the lungs, although high ACE2 and low DPP4 expression were detected in nasopharyngeal cells.

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is likely to have originated in bats and spread to humans through intermediate hosts.

IDENTIFICATION OF POTENTIAL INTERMEDIATE HOSTS - DATA FROM SOUTH ASIA

In another significant research project, BARJ team used silico (computer-based) approaches to predict the potential hosts and intermediate hosts of SARS-CoV-2. They conducted diversity analysis of ACE2 and transmembrane protease serine 2 (TMPRSS). ACE2 acts as a cellular receptor for SARS-CoV-2, while TMPRSS helps in...
spike protein priming. Phylogenetic (evolutionary development) trees based on the amino acid (aa) sequences of ACE2 and TMPRSS2 were created for this purpose. Human ACE2 was found to be clustered with rhesus macaques but separated from mouse and rat ACE2. In these trees, members of the Bovidae family, such as cows, buffaloes, goats, and sheep formed a cluster, while all the bird species clustered with chicken. In this study, they also stimulate the structure of SARS-CoV-2 RBD (receptor-binding domain of SARS-CoV-2 spike protein) with ACE2s. It was performed to investigate their binding affinity and identify potential intermediate animal hosts responsible for spreading coronaviruses to human in South Asia. Based on the recently solved crystal structure of the SARS-CoV-2 RBD in complex with human ACE2, they identify 20 possible a possible intermediate host in SARS-CoV-2. FUTURE PERSPECTIVE: Data from the differential transcriptome study can provide new insights into the response of hosts against the virus from different parts of the respiratory tracts. Despite the fact that this research only includes a small number of cases, the findings can aid in the development of future studies to elucidate the different host responses to viral pathogenesis. With further research, more data can be incorporated and enrich the quest for effective therapeutics. The findings of the potential intermediate host study can provide a valuable resource for identifying possible hosts for SARS-CoV-2 in South Asia. With proper management of potential and intermediate hosts, the risk of a COVID-19 outbreak in the future can be reduced.

Rhesus macaque was the only species, with 100% similarity to human ACE2, to be as susceptible to SARS-CoV-2 as humans.

References


Personal Response

Do you have any plans to utilise data from your own studies and develop effective therapeutic strategies to fight COVID-19, given that many countries around the world are experiencing a second wave?

At the time we started this work there was no available genome sequence of SARS-CoV-2 from Bangladeshi isolates. This SARS-CoV-2 genome sequence provides the research community an opportunity for diversity analysis and molecular characterisation of SARS-CoV-2 from Bangladeshi patients. Our goal is to support the health and medicine sector of Bangladesh, who conducts research to develop effective therapeutic strategies to fight COVID-19. Although our centre largely focuses on research into the jute genome and the improvement of jute varieties, we are ready to provide any type of support to the research effort associated with COVID-19 for the betterment of mankind.