Structural and functional implications of non-synonymous mutations in the spike protein of 2,954 SARS-CoV-2 genomes

A team of Scientists at Corona Research & Intervention Group at DBT's Rajiv Gandhi Centre for Biotechnology (RGCB), Thiruvananthapuram have studied structural and functional implications of non-synonymous mutations in the spike protein of 2,954 SARS-CoV-2 genomes**.** Since, the SARS-CoV-2, the causative agent of COVID-2019 pandemic, is an RNA virus prone to mutations, the information on mutations within the circulating strains of the virus is pivotal to understanding the disease spread and dynamics.

Dr. Shijulal and team at RGCB have analysed the mutations associated with 2,954 globally reported high quality genomes of SARS-CoV-2 with special emphasis on genomes of viral strains from India. Molecular phylogenetic analysis suggests that SARS-CoV-2 strains circulating in India form five distinct phyletic clades designated R1-R5. These clades categorize into the previously reported S, G as well as a new unclassified subtype. A detailed analysis of gene encoding the Spike (S) protein in the strains across the globe shows non-synonymous mutations on 54 amino acid residues. Among these, the research team pinpointed 4 novel mutations in the region that interacts with human ACE2 receptor (RBD).

Further *in silico* molecular docking analyses suggested that these RBD mutations could alter the binding affinity of S-protein with ACE2 that may lead to changes in SARS-CoV-2 infectivity. Strikingly, one of these RBD mutations (S438F) was found unique to a subset within the R4 clade suggesting intrinsic S-protein variations in strains currently circulating in India. The research team's findings revealed a unique pattern of SARS-CoV-2 evolution that may alert vaccine and therapeutic development.

Link: https://www.biorxiv.org/content/10.1101/2020.05.02.071811v1

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