Snake Venom Peptides and Toxin targeting the Main Protease of SARS-CoV-2

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The corona virus began to spread in Wuhan, China which caused it to spread worldwide creating a global pandemic in the beginning of 2020, infecting over 243 million and killing over 4.5 million people worldwide. Significant efforts were made to produce vaccines against the virus, which led the recognition of a few vaccines that has been approved by FDA. These vaccines, Pfizer-BioNTech, Moderna and Johnson & Johnson, which all have efficacy against Covid-19. Despite having vaccines, COVID-19 is still present and infecting millions and killing thousands of people every day. Multiple therapeutic options would allow us to slow down or even stop this pandemic.

Snake venom peptides are known to have antiviral and antimicrobial properties. In this study, we have performed computational screening of well-known venom peptides OHCATH (KF-34), Cathelicidin (BF-30), Lycotoxin I (IL-25), and Lycotoxin II (KE-24) as well as 50 venom and toxin peptides against the main protease (Mpro/3CLpro) of SARS-CoV-2. The 3CLpro protein acquired attention because of its crucial role in post-translational processing of replicase polyproteins and viral replication. The venom and toxin peptides contain 7 to 34 amino acids. These peptides were modelled using PEP-Fold where sequence was used as an input. To perform molecular docking between 3CLpro and peptide, initially PATCH-DOCK was used. The clusters obtained from PATCH-DOCK were further refined by FIRE-DOCK. The Peptides with the highest binding affinity also interact with the active site residues such as His41 and Cys145. Cathlecidin (BF-30), Lycotoxin I (IL-25), and Lycotoxin II (KE-27) displayed the highest binding affinity ranging from –63.73 to –41.28 kcal/mol. Various nonbonding interactions such as hydrogen bonding and hydrophobic interactions are detected in peptide–3CLpro complexes. The best peptides will undergo molecular dynamics simulations followed by protease assay and native mass spectrometry experiments.