BIO-PLEX: An Innovative Biocomputational Approach to Decode the Secrets of the 2022 Mpox Resurgence

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In mid-2022, Mpox reemerged with heightened infectivity and transmissibility, causing 30,000 cases in just six months. As we recovered from COVID-19, fear of another pandemic heightened. Two fundamental questions emerged: What caused Mpox to increase its infectivity, and what structural changes might have contributed? Will changes in the protein structure affect the efficacy of drugs? A major bottleneck was the lack of three-dimensional structures for Mpox replication complex. Experimental studies can take years to answer these questions. By using biocomputational methods, we can get answers in a significantly shorter time. So, I developed "BIO-PLEX," —an innovative biocomputational pipeline that uses a unique combination of deep-learning and homology modeling through a lego-brick approach and Python mutation profiling. BIO-PLEX can decode the structure of multi-protein complexes (e.g., Mpox replication complex) and their mutations to predict the causative factors of higher infectivity. My investigation consisted of three objectives using BIO-PLEX: 1. predicting structure of Mpox replication complex, 2. identifying mutations in the virus that appeared in the outbreak, and 3. identifying causative factors for increased transmissibility and effectiveness. Among five components of the minimal replication complex, ten mutations were observed. Two mutations, L108F and W411L, in DNA polymerase play a critical role. Notably, L108F in DNA polymerase protein (only in the current outbreak) increases binding affinity between protein and DNA. Both mutations could be crucial to the virus's infectivity. I also identified mutational regions in the Mpox virus that could confer resistance. Mpox is a case study for BIO-PLEX, which can be applied across many outbreaks and future viruses.

Awards Won:

First Award of $5,000

Regeneron Young Scientist Awards