

## THE USE OF AI AND ADVANCED COMPUTER SYSTEMS TO DEVELOP DRUGS AGAINST NEW EMERGING THREATS

### Machine Learning Models To Identify Egg-adaptive Mutations For Rapid Vaccine Virus Development

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Vaccination is the most effective medical countermeasure to combat novel and recurring biological threats. While vaccine development has become more efficient over the past decade, the best example being the recently created mRNA vaccines for SARS-CoV2, it is still a slow and inefficient process for many agents. For example, influenza is a threat to both public health and service members alike, but development of influenza vaccines involves arduous and time-consuming screens for variants that increase replication in chicken eggs, the most common vaccine production platform. This process can take months and introduce unintended mutations that alter vaccine efficacy. Methods to accelerate the identification of egg-adaptive mutations are therefore essential to decrease the time between detection and countermeasure creation. Machine learning offers one promising avenue for rapid identification egg-adaptive mutations. Here, we used nearly 60,000 viral genomes to construct a series of machine learning models able to distinguish egg adapted H3N2 and H1N1 strains with a high degree of reliability (F1 scores > 0.90), indicating strong and detectable differentiation between adapted and non-adapted viruses. These models also identified context-dependent mutations in the hemagglutinin gene that could be introduced into viruses to improve vaccine production. Many of the mutations identified have well-documented roles in egg-adaptation, such as G222D and G186V/S193F. Other mutations, like D225G, however, are less well-known, highlighting the need for further research in even the most well-studied vaccine virus systems. This work will make virus development more efficient and cost effective, furthering JSTO's mission to advance the world of medicine, and helping create safeguards against biological threats for both warfighters and the nation.