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ABSTRACT BOOK

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0605

IMMUNOLOGICAL EVALUATION AND COMPARISON OF DIFFERENT CACHE VALLEY VIRUS VACCINE CANDIDATES

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Cache Valley virus (CVV; genus *Orthobunyavirus*, family *Peribunyaviridae*), first isolated in Cache Valley, Utah in 1956, is now enzootic throughout the New World. Although transmission of CVV occurs through an enzootic cycle including more than 30 species of competent arthropod vectors, serological evidence has indicated white-tailed deer as the amplification host for the virus in nature. Whilst CVV is primarily known to cause severe disease in pregnant ruminants resulting in abortions, fetal malformations, and embryonic lethality, it has also been recently recognized for its expansion as a zoonotic pathogen. Other viruses in the bunyamwera serogroup are thought to be of minimal concern. However, during an outbreak of Rift Valley fever virus, Ngari virus was found to have infected some of the goats being tested, and Oropouche virus, has been responsible for febrile disease outbreaks in Central and South America. With this increased emergence of bunyaviruses with human and veterinary health importance, there have been significant efforts dedicated to the development of bunyavirus vaccines. In this study, immunogenicity of a CVV vaccine candidate based on the deletion of NSs and NSm genes was evaluated and compared to a vaccine candidate created through the inactivation of CVV using binary ethylenimine with the addition of an aluminum hydroxide adjuvant in sheep. Immunization of 20 sheep with one of the two vaccine candidates was performed followed by two booster immunizations. Plaque reduction neutralization test was then used to monitor the development of neutralizing antibodies elicited by each vaccine candidate. The development of a vaccine for ruminants could lead to less human exposure and a platform for CVV and other emerging bunyaviruses that have already or could potentially cause future outbreaks.

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ENSEMBLE MACHINE LEARNING METHOD AS A HIGH ACCURACY APPROACH TO COVID-19 SIMULATION

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The COVID-19 pandemic shows that only timely implemented scientifically based measures can stop it. Mathematical modeling is an effective tool for studying the epidemic process. However, models suffer from low accuracy and are short-term in nature. Ensemble machine learning methods help optimize predictive models by combining several base models of epidemic processes. Different modeling approaches have different disadvantages, but their combined use makes it possible to eliminate these drawbacks. We used ensemble machine learning models to see if we could improve the accuracy of COVID-19 morbidity forecasting using data provided by the Coronavirus Resource Center of John Hopkins University & Medicine. The result was a cluster analysis method grouping countries based on similar COVID-19 morbidity characteristics, forecasting COVID-19 morbidity for each group using neural network, and combining the results into one country database. For clusterization we developed a neural network with 60 input neurons, 100 hidden neurons with Fermi activation function, and 4 output neurons. For forecasting, a neural network was built with 6 pairs of layers Dense with an activation function ReLu and 64 neurons, a layer Dropout and the last layer Dense with one output, RMSProp method as optimizer and Mean Squared Error as error function.

The final ensemble machine learning model was realized using Python programming. Employing ensemble machine learning model, we improved the accuracy of the forecast of COVID-19 morbidity to 98.11% compared to other models with accuracy of 85.12% (compartment models) or 87.30% (machine learning based models). High accuracy forecasting will improve the investigation of short-term dynamics and long-term trends of COVID-19 epidemic processes. In turn, this will allow for timely implementation of scientifically grounded measures to decrease COVID-19 dynamics. These results indicate that ensemble machine learning is useful tool for understanding the main drivers of COVID-19 dynamics and may better inform decision-making processes to prevent new waves of morbidity and deterioration of the epidemic situation.

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COVID-19 SEROSURVEYS IN MASSACHUSETTS: CALL FOR ACTION

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Seroprevalence studies (i.e. serosurveys) are essential public health tools that help determine the extent of an infectious disease outbreak and map its distribution among specific populations. COVID-19 serosurveys are particularly important, because (i) they capture asymptomatic infections, which are thought to account for 40-45% of all SARS-CoV-2 infections, and (ii) they indicate the level of existing immunity among affected populations. We implemented a laboratory developed test (LDT) that measures IgM, IgG and IgA antibodies by ELISA against the SARS-CoV-2 Spike Receptor Binding Domain (RBD) to determine the seroprevalence among health care workers (HCW) and return-to-work employees (RTW) at the University of Massachusetts Medical School. We enrolled and collected blood from 553 HCWs between April 27 and June 4, 2020 and 335 RTWs between Aug 3 and Aug 6, 2020. Our initial findings based on RBD IgG antibody levels, which is the most specific compared to PCR-confirmed cases, found a 14.1 % and 5.3 % seropositivity among HCWs and RTWs, respectively. The correlation between IgG and IgA levels was modest (r=0.4, Spearman Correlation, p<0.0001), supporting other studies that have shown divergent development of IgA in lieu of IgG for this respiratory infection. In contrast, IgM was the least sensitive and specific as a serosurveillance metric. As expected, we found that the overall positivity was higher among HCWs who were at higher risk of SARS-CoV-2 exposure as compared to employees who had been working remotely. This LDT ELISA has also been adapted for nucleocapsid and spike trimer protein in order to compare the sensitivity and specificity of each antigen and isotype, alone and in combination. In summary, we found that most of the HCWs and RTWs who enrolled in our study did not have antibodies to RBD, emphasizing the need for vaccines in order to reach population-wide immunity. This study shows that it is possible for academic medical centers to rapidly deploy LDTs and contribute to public health surveillance strategies for COVID-19.

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