Marek's Disease and Its Outbreak in Asia: Python-Based Approach for Detection of Marek's Virus

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Marek's disease is an infectious disease that manifests in tumors of the nervous system and organs in chickens. Computer programming languages have enough potential to detect various viral diseases. An effort has been made to detect and evaluate the intensity of viruses. Despite the widespread use of effective vaccines designed to halt its spread, recent data reveal that their efficacy is declining as a result of the virus's adaptability. We analyzed 53 reports documenting 157 viral strains in Asian countries during the last decade of Marek's disease outbreaks and correlated meq sequences. The visceral variety of Marek's disease is the most common (18 out of 28 investigations), although there may be other, unrecognized brain alterations as well. Most commonly, MD causes tumors in the liver (16 out of 26 studies), however, other organs such as the spleen, kidney, heart, gizzard, skin, gut, lung, and sciatic nerve have also been affected. Using amino acid alignment, we found numerous point alterations in 28 strains that may be associated with its virulence. More research is needed on the virulence of the Marek strain, as well as the structural modifications to the Meq protein, and we recommend that this research take place in disease-endemic areas.

Keywords: Marek's Disease, Outbreak, Pandemic

Introduction

Despite widespread usage of vaccines during the past decade, Marek's disease continues to cause economic loss throughout Asia. This article attempts to provide a comprehensive overview of the recent epidemiological, virulence-related meq gene variation, and pathological data on Marek's disease in Asia. We discovered that 157 distinct viral strains, each with a unique meq sequence. We observed that 18 different strains in China were resistant to vaccines, with mortality rates of thirty percent or more. This data mandates that the relevant area in China represents the immunization strategy; nevertheless, more research is required regarding the efficacy of vaccination in other Asian countries, as the available data is insufficient. The visceral tumor is the most common pathological kind in Asia while a neurological type might also exist. For early detection of this dangerous disease, we recommend that farmers keep an eye out for changes in chicken behavior. Geologically related countries in the Middle East, South Asia, and East Asia are shown to be linked in a phylogenetic analysis, therefore managers of chicken trading operations in these regions should be aware of the risk of viral transmission.

The chicken sector faces serious danger from Marek's disease (MD). Mortality rates for afflicted chickens have been reported anywhere from 20% to 65% since the disease's discovery in a Hungarian chicken farm in 1907. Despite progress in vaccine development and clinical monitoring, MD still results in an annual economic loss of almost USD 1 billion [1]. Initially, clinical pathology identification and then genetic confirmation is used for monitoring MD in farms. Neural and visceral versions of the disease can be distinguished [2], with respective death rates of 10-25% and >70%. The main clinical symptoms of neural MD include weakness or paralysis of the neck, wings, and limbs. Increased size and a yellowish hue characterize lesions of the vagus, brachial, and sciatic plexuses, which are the most common causes of such paralysis. Edoema and inflammation are typically shown as vacuolar degeneration in the nerve parenchyma and infiltration of mononuclear cells in histological sections[3]. Grey or foggy eyes, small tumors in the ovary, heart, liver, lung, and other organs, and, typically, iridocyclitis and lymphomas revealed further under microscopic observation are all symptoms associated with more severe infections. Visceral MD is characterized by the presence of significant numbers of tumors in multiple organs, including the gonads, liver, kidney, lung, heart, spleen, and proventriculus[4]. Lymphoid carcinoma typically forms in these nodules[5][6]. It is crucial to identify the predominant strain during outbreaks so that the disease may be tracked more effectively.

Marek's disease (MD) is an infection caused by the alpha herpesvirus, Mardivirus genus member Marek's disease virus (MDV), also known as Gallid alphaherpesvirus 2 (GaHV-2). There are three distinct stages of MDV infection: cytolytic, latent, and T-cell transformation. To generate widespread tumorigenic T cells, MDV multiplies extensively in CD4+ T cells and produces an oncogenic transformation [7][8]. The efficiency with which lymphoma cells can be produced (oncogenic transformation potential by MDV) and their transmissibility largely determine the severity of the disease and, by extension, the likelihood of death [9]. The genetic potential for transformation has been investigated. There are four types of inverted repeats in the MDV genome: terminal repeat long (TRL), internal repeat long (IRL), unique short (US) region, and inverted short repeats. A particular meq gene, 1020 base pairs in length, was found to be located in both the TRL and the initial left and right ends of the genome [10], and this gene produces a 339 amino acid long protein called meq. Like other members of the Jun/Fos family of activators, the Meq has a basic region-leucine zipper domain. Using this domain,

Meq can create a heterodimer with c-Jun proteins or with itself [11]. This heterodimer then activates Jun, Fos, and ATF/CREB family proteins, leading to increased expression of IL-2 and CD30 [12]. Life Cycle of Marek's Disease is showing in Figure 1.

Life Cycle of Marek's Disease

In Hodgkin's disease, these two variables have been shown to cause lymphomas in the past [13]. In addition, binding induces cyclin-dependent kinase 2, which can cause P53-RB pathway-mediated dysregulation of cell cycle control [14]. Also, recent research has shown that Meq can bind the main regulator of cell cycle entry and proliferation metabolism protein Myc [15]. Reducing the efficiency with which tumor cells are eliminated, this interaction with Meq inhibits the function of these two proteins, which are important regulators of viral telomerase RNA (vTR)-induced apoptosis. Since mutations in the meq gene have been shown to cause distinct virulences in MDV strains, meq sequencing has emerged as a crucial marker of MDV virulence and strain classification [16].

Vaccination is an effective method for preventing MD symptoms in hens. Protective indices of more than 90% were seen in an early investigation of the three well-known vaccinations based on strains SB-1, CV1988 (Rispens), and FC126; these vaccines have greatly shortened global outbreak times over the past 30 years [17][18]. However, some contend that MDV's continued spread among infected people could aid in the evolution of the virus, ultimately leading to more virulent strains with increased rates of reproduction[19]. Studies have shown that CVI1988 is not as effective against some emerging strains, prompting calls for an epidemiological assessment of the disease's current prevalence [20]. Some of the worst cases of MDV infection occur in Asia and other Asian countries. Viruses like CVI1988 have a long history of infecting hens in places like China, Japan, and India, and new viral strains are reported virtually year [21]. Many studies demonstrate that the incidence rate of MD in Asia is rising and that new outbreaks are frequently connected to new virulent strains, despite the widespread use of vaccine injection, notably for CVI1988 and HVT [22]. The precise position of MD in Asia over the past few years is, however, still poorly understood. How does the pathology of the disease manifest? How dangerous are the most recent MDV strains? How do variations in meq sequences affect these strains? How effective are the immunizations that are typically administered? This research looked at the most recent ten years of data for these indices to determine if vaccine and strategy renewal was necessary.

This review looked for articles published between 2010 and 2022 that included Marek's disease, Marek's disease virus, or poultry in Asia. We included articles with at least one piece of data on MD pathology, virus identification, virulence estimation, prevalence, and mortality throughout Asia, including research, reviews, and case reports. After that, all of the collected data were examined for signs of patterns or epidemics[23] [24]. Annotations were added to the final studies to describe the outbreak and study years, the locations of the infected farms, the rates of MD incidence and death, the availability of vaccination, the types of pathology found (visceral versus neural), the viral strain isolated, and the method used to identify the virus[25].

Novelty Statement

An effort has been made to develop a python based script for detection of Marek's virus.
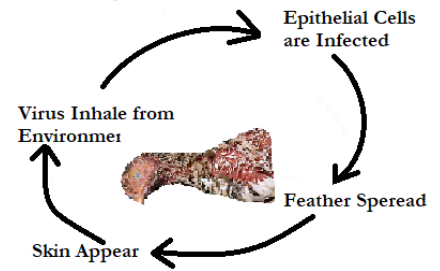
Analyses of the Phylogeny

To ensure that no indel mutations were missed during alignment with MEGA X, all sequences from publications (29 of 36 studies) with detailed meq sequence information or available viral strain meq information were exported and checked for accuracy and length according to the sequence information [26] [27]. The problem was probably caused by an incomplete or incorrect upload[28]. After the data was aligned, to perform a phylogenetic test using a bootstrap sample size and to determine evolutionary distances using the neighbor-joining method.

Discussions and Results

From different regions, including Bangladesh, China, India, Indonesia, Iran, Iraq, Japan, Malaysia, Pakistan, Saudi Arabia, South Korea, and Turkey, a total of 48 studies were compiled about the 309 farms that were found to have MD outbreaks. These investigations reported a neural type, which show that the liver was the most common site where MDV-induced lymphoma developed (12 studies), followed by the spleen, the bursa of Fabricius, the kidney, the skin, the heart, the gizzard, the intestine, and the lungs. Lymphoma was found in the sciatic nerves, one of the four types of nerves studied. Depending on the types of viruses involved and whether or not people were immunized, fatality rates from MD ranged from 1% to 78%, We observed that strains from China were able to avoid the protection of the CVI988 vaccination, leading to a death rate of over 40%, by analyzing data from farms, or conducting experimental studies. Over half of the population was lost in seven these situations.

We used the Meq sequences to undertake a phylogenetic analysis of the 140 viruses and the CVI1988 strain. More than 86% of the viruses found in Turkey, Iraq, Iran, and Saudi Arabia have less than 10 base pair differences between them, indicating they likely share a common ancestor. Less than three base pair variations were detected between strains from Turkey, Iran, and Saudi Arabia. This indicate that the virus was being transmitted between Turkey and India. The viruses in China can be roughly classified into three families based on their genetic sequence That shows that the "China Group 1" (the red branch) is responsible for the majority of recent outbreaks. The second group is the "China Group 2" (brown branch), which shared very few mutations (less than three) with the vaccination strain CVI988. Finally, "China Group 3" (purple branch) is related to "2014-2015 Japan Kgs-C1" and "2014 Indonesia SMI14-KampungCk" (both in red). Furthermore, there are some outliers: the "2015 China Crane" strain, isolated from a wild crane, showed more similarities with "2011-2015 China HS/1412", "2016 China An-1", and the "India Group 2" (yellow branch,) than with China Groups 1, 2, and 3, suggesting that there may have been two branches of MDV evolution in China. There are two main clusters of Indian strains; "India Group 1" (the green branch) and "India Group 2" (the yellow branch). The first set was determined to be more similar to the "2015 China Crane branch," while the second was found to be more similar to the "2014 Indonesia SMI14-KampungCk." The "2016 Japan Gifu1-6" and the "2014-2015 Japan Me-C3" strains were also isolated in Japan, and they shared very little genetic material with any other strains (more than 10 point mutations separated them from each other). We were able to classify the world into three interconnected regions based on the groups and evolutionary distances: the Middle East (Turkey, Iraq, Iran, and Saudi Arabia), South Asia (India and Indonesia), and East Asia (China Group 3). There were less than 10 distinct point mutations across strains originating from inside the region's individual countries. However there is also a "China Group 1" and a number of severely altered viruses that have been mostly discovered in Japan.

Programming Approach

Programming languages can be used in conjunction with various techniques and tools to aid in the detection of chicken viruses, including Marek's disease virus. Here's an approach of how programming languages can be applied in context of virus detection.

Use programming languages such as Python, it is easy to collect and preprocess relevant data. This may include genetic sequences, clinical data, laboratory test results, or any other information that can help in virus detection. Python libraries like pandas can be useful for data manipulation and preprocessing tasks. Extraction of informative features from the collected data using programming techniques may involve analyzing genetic sequences, extracting statistical features, or applying domain-specific algorithms to derive relevant features for virus detection.

Various libraries including scikit-learn, TensorFlow, or PyTorch provide an easy way to implement machine learning algorithms for virus detection. These libraries are trained to evaluate models using the collected and preprocessed data. Techniques such as classification, clustering, or anomaly detection can be applied depending on the specific virus detection requirements. Programming scripts or applications that integrate with diagnostic tools are commonly used in virus detection. These tools may include PCR analysis, ELISA, or other laboratory techniques. Programming languages can be used to automate data processing, analysis, and interpretation of results obtained from these diagnostic tools.

Create visualizations and reports using programming languages to communicate the detection results effectively. Python libraries like Matplotlib or seaborn can be employed to generate informative graphs, charts, or heatmaps for visual analysis. Develop programs or scripts continuously monitor chicken populations for virus detection. These programs can integrate with sensors, IoT devices, or data streams to provide real-time monitoring and alert systems. Programming languages such as Python, Java, or C++ can be used for these purposes. It's crucial to collaborate with domain experts, veterinarians, or researchers who possess the knowledge and expertise in chicken virus detection. They can provide guidance on the appropriate programming techniques, algorithms, and diagnostic tools specific to the virus you are targeting. We developed the following python based program for detection of Marek's disease.

```
import numpy as np
import pandas as pd
data = pd.read_csv('virus_dataset.csv')
from sklearn.model_selection import train_test_split
X = data.drop('label', axis=1)  # Features
y = data['label']  # Labels
X_train, X_test, y_train, y_test = train_test_split(X, y, test_size=0.2,
random_state=42)
# Step 5: Choose and train a machine learning model
from sklearn.ensemble import RandomForestClassifier
model = RandomForestClassifier()
model.fit(X_train, y_train)
# Step 6: Make predictions on the testing set
y_pred = model.predict(X_test)
# Step 7: Evaluate the model
from sklearn.metrics import accuracy_score, precision_score, recall_score, f1_score
```

```
accuracy = accuracy_score(y_test, y_pred)
precision = precision_score(y_test, y_pred)
recall = recall_score(y_test, y_pred)
f1 = f1_score(y_test, y_pred)
print(f"Accuracy: {accuracy}")
print(f"Precision: {precision}")
print(f"Recall: {recall}")
print(f"F1-score: {f1}")
dump(model, 'virus_detection_model.joblib')
loaded_model = load('virus_detection_model.joblib')
new_data = pd.read_csv('new_data.csv')  # Load new data
predictions = loaded_model.predict(new_data)
```

Our devised model is capable to detect Marke's virus by loading certain libraries. Marek's disease is a highly contagious viral disease that primarily affects chickens. While there is no cure for Marek's disease. There are several preventive measures to take to minimize the risk of the disease spreading and to protect your poultry flock.

Preventive Measures.

Vaccination is an essential preventive measure against Marek's disease. Consult with a veterinarian to determine the appropriate vaccination program for your flock. Vaccinating chicks at an early age can help provide protection against the disease.

Biosecurity: Implement strict biosecurity measures to prevent the introduction and spread of Marek's disease on your premises. This includes limiting visitors, using dedicated footwear and clothing when entering poultry areas, and disinfecting equipment and vehicles. Maintain separate areas for newly acquired birds or those from unknown sources until their health status is verified.

Practice good hygiene and sanitation within your poultry facilities. Regularly clean and disinfect the premises, equipment, and water sources. Proper waste management is also crucial to reduce potential disease transmission. Quarantine new birds before introducing them to the existing flock. This allows for observation and testing to ensure they are free from Marek's disease and other infections. Quarantine periods typically range from a few weeks to a few months. Separate chickens into age-appropriate groups to minimize the risk of disease transmission. Young birds are more susceptible to Marek's disease, so keeping different age groups apart reduces the chance of viral spread

Implement measures to control rodents and other pests, as they can act as vectors for disease transmission. Properly store feed and dispose of spilled feed to deter pests. Consider genetic selection when acquiring new birds. Some chicken breeds have varying levels of resistance to Marek's disease. Choosing breeds or strains that have been bred for resistance to the disease may help reduce the risk.

Regularly monitor your flock for any signs of illness or abnormalities. If any birds exhibit symptoms suggestive of Marek's disease, promptly isolate and seek veterinary advice for diagnosis and appropriate measures. Stay updated on the latest information, research, and best practices related to Marek's disease prevention. Attend workshops or seek guidance from poultry experts or veterinarians to enhance your understanding and implementation of preventive measures.

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