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平成２８年度研究助成（海外渡航費）研究成果報告書

平成 29 年　3 月　23 日

公益財団法人遺伝学普及会 代表理事　殿

貴財団より助成のありました研究の成果を下記のとおり報告します。

海外渡航者氏名　KAWASHIMA Kent Diel

出席学会等名称　2016 International Meeting on Emerging Diseases and Surveillance

開催場所　Vienna, Austria

開催期間　平成 28 年 11 月 3 日 ～ 平成 28 年 11 月 7 日

渡航期間　平成 28 年 11 月 2 日 ～ 平成 28 年 11 月 8 日

研究成果の概要

The International Meeting on Emerging Diseases and Surveillance is a biennial gathering of scientists, researchers, medical doctors and veterinarians to discuss the latest efforts to track and mitigate the spread of infectious diseases as well as to learn about the latest research on the pathology, mechanism, and available treatment for communicable diseases in humans and animals. This year, the conference hosted more than 600 participants from all over the world coming from different scientific and medical backgrounds consistent with the conference's emphasis of the "One Health" approach. One Health is the concept that people's health is intrinsically tied to the health of animals and the shape of the environment. Given that 6 out 10 infectious diseases in humans come from animals, the One Health approach advocates collaboration across disciplines in order to achieve the best health for people, animals and the environment.

At the conference, I presented my work entitled "The global population genetics of Dengue viruses revealed through temporal and spatial mapping of viral genetic variation". The purpose of my study was to reveal the fine-scale molecular evolution of Dengue viruses worldwide across time by building a comprehensive database of viral genetic variation coupled to temporal and geographical information. I envision this integrated map could help track not only the spreading of Dengue disease, but for other types of infectious disease pathogens such as Influenza, Malaria, and HIV. Many participants also shared this opinion regarding the importance of using genetic data in combination with epidemiological information and would like to have a similar database and visualization tool to use for their study. Interestingly, I also had the opportunity to talk to medical doctors, and they too found the usefulness of population genetics concepts to understand the distribution of viral genotypes in terms of how it could affect the severity of infections and the size of outbreaks. With the goal of "One Health", I realized that it is important that researchers like myself also collaborate with medical doctors and scientists from other fields to create meaningful knowledge for better public health.

Based on the feedback from researchers working with Dengue viruses as well as scientists working on other vector-borne diseases, I will be making the database and the tools publicly available so that many more people can benefit from using it. In the future, I hope that the tools I created to understand Dengue viral variation can also be applied to many more different kinds of pathogens to better understand how evolution of these infectious agents affect disease severity and outbreak potential.

The global population genetics of Dengue viruses revealed through temporal and spatial mapping of viral genetic variation

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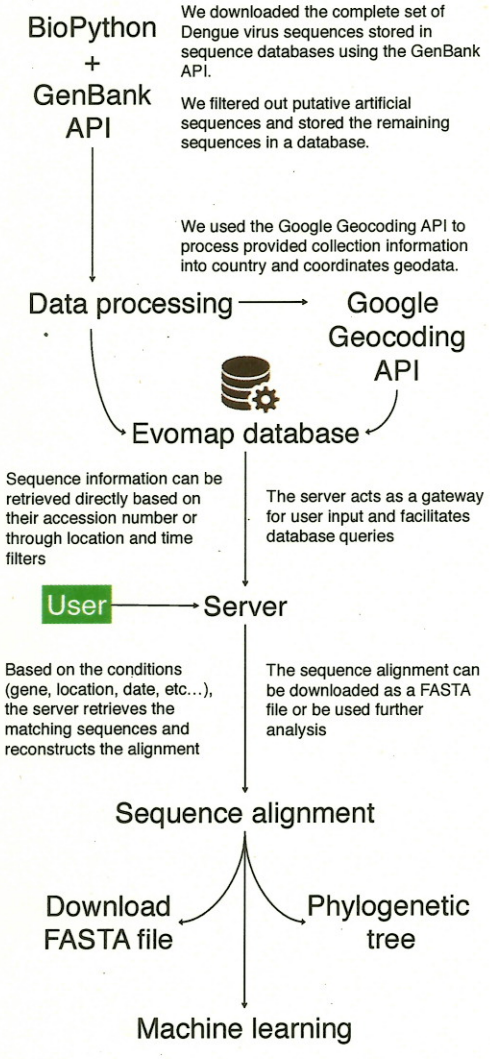
Introduction

Dengue viruses are a genetically diverse group of mosquito-borne RNA viruses that cause more than 300 million infections yearly worldwide. Numerous phylogenetic studies have shown that within each Dengue virus serotype, viruses cluster into Asian and American lineages based on their sequence similarity indicating the major role geography plays in the population structure of Dengue viruses.

However, the precise genetic variation that determine these groups, the frequencies and distributions of variants and the reasons behind these observed polymorphisms remain poorly understood and complicated by rapid molecular evolution of the viral genome.

To better understand the relationship between genetic polymorphism and geography over time, we constructed a comprehensive database and analysis pipeline to link genetic information and collection metadata to reveal the emergence and global flow of viral genetic variants.

Software framework



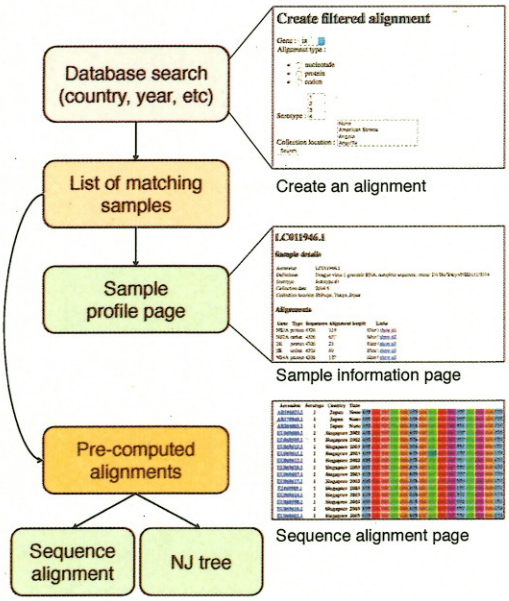
We used machine learning modules in Scikit-Learn to find patterns in sequences and to determine relationships between sequence and metadata.

Results and Discussion

Sample workflow

Find samples that were isolated in a particular location and/or time interval

Samples and their sequences can be retrieved based on a list of countries where samples have been isolated from. More advanced search is also possible, such as retrieving by address (region, country, etc.) or spherical coordinates (latitude and longitude) via a geocoding API to parse and segment an address into street, city, region, and country data. Sequences can also be retrieved by year or by specifying a time interval.



Create Alignments

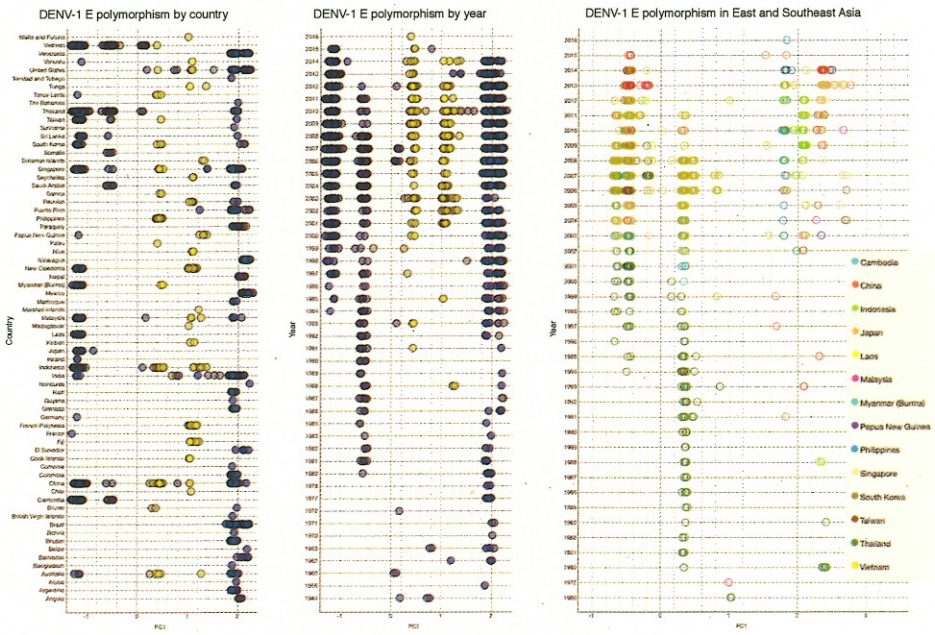
Alignments are pre-computed using MAFFT and stored when a sequence is inserted into the database. Since each row is associated to its corresponding sample, we can filter alignment based on sample metadata such as location and time of isolation, and sample serotype. Based on the search criteria, the system returns only the matching alignment rows.

Given the retrieved alignment, the system computes summary statistic such as number of sequence, alignment length, GC content, and genetic diversity.

A neighbor-joining tree can also be constructed from the retrieved alignment using pre-computed pairwise DNA and protein distances.

Tracking genetic polymorphisms through space and time

We demonstrate how we can track the distribution of Dengue virus haplotypes over a period of time using the Evomap database. Here we show the global and regional distribution of DENV-1 envelope protein sequences using principal components analysis to how genetic variants distribute across geography and time.



Conclusion

We have compiled a comprehensive database of viral genetic variation tied to temporal and geographical information to reveal the fine-scale molecular evolution of Dengue viruses worldwide across time. Our integrated map will help track the global spreading of Dengue virus variants to retrace the source of outbreak in new locales and reveal the effect of nascent Dengue vaccination on viral evolution.