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学位の種類	博士(工学)
学位記番号	シス博 第67号
学位授与の日付	平成27年9月30日
課程・論文の別	学位規則第4条第1項該当
学位論文題名	Development of New Diagnostic Tools for Effective Public Health Action in the Prevention and Control of Infectious Diseases in Southeast Asia (東南アジアにおける感染症の予防と制御に対する効果的な公衆衛生学的対応のための新たな診断ツールの開発)
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【論文の内容の要旨】

Diagnostic capacities must be built and sustained in Southeast Asian countries to detect and to anticipate the emergence of infectious diseases. This will allow effective and timely public health action to be implemented for the prevention and control of infectious diseases. The objectives of this dissertation were to develop newer diagnostics tools to be used in the detection of infectious diseases which can be used to generate infectious disease information that will be crucial in the implementation of effective public health action for the prevention and control of infectious diseases in Southeast Asia. In order to achieve these objectives, investigations of the nature of infectious diseases in Southeast Asia were carried out. Specifically, a new method for the rapid and total characterization of viruses was developed. Serologic diagnostic test for an emerging virus affecting Southeast Asia was developed and used in a population survey in Southeast Asia. To support these investigations, new diagnostic tools were developed. These new tools with microstructures reduced the total time and volume of samples needed for the diagnosis of infectious diseases. In addition, a portable disease diagnostic system for rural and onsite testing was utilized to generate infectious disease information. The newly developed method for the characterization of virus was applied in the investigation

of a new virus affecting Southeast Asia, namely Pteropine orthoreovirus (PRV). This new method reduced the total time and effort required to complete the investigation of PRV and showed crucial information on the existence of PRV in Southeast Asia. Although human infections with PRV are mild, the use of the newly developed serologic test showed that humans in Southeast Asia are at risk of infection with PRV. These experimental findings also showed the first evidence of human infection with PRV in Vietnam. The newer diagnostic tools developed were used in the detection of infectious diseases in Southeast Asia and showed an increased sensitivity with the potential to reduce time and volumes compared to the standard methods. These are crucial considerations for the uptake of diagnostic tools in resource-limited settings like Southeast Asia.

This thesis is composed of five chapters. The introduction and main achievements of this Study are summarized below.

Chapter 1 introduces the background of infectious diseases in Southeast Asia and the current methods to detect them. The limitations in the present methods are mentioned and approaches in overcoming them are indicated. Based on the issues in infectious disease detection in guiding public health action in Southeast Asia, the motivation and objectives of this study are stated.

Chapter 2 investigates the nature of infectious diseases in Southeast Asia. A new method to characterize PRV was developed and used in investigating the nature of PRV infection. This method reduced the total time required to complete the investigation from at least 6 months to less than 1 week. Serologic methods were also developed that showed that human infections with PRV are more common than previously known. These assays can be used to detect a change in nature of PRV from mild to potentially fatal cases. This method was validated through a population-based survey carried out in Central Vietnam which showed the first evidence of human infection with PRV. This method also showed that human infection and possible reinfection with different PRV strains is geographically more distributed in Southeast Asia and future investigations must be continued to monitor a change in this virus, should a change in its virulence occur.

Chapter 3 investigates the development of new tools for the diagnosis of infectious diseases in Southeast Asia. Tools with microstructures were developed using 3D printing and commonly available fabrication technologies, namely nanoimprinting and press stamping. The cycles of designing to prototyping to assessment were feasible and rapid. These newer tools were designed with an increased surface area of up to 6-times more compared to the conventional 96-well. From a diagnostic aspect, these

tools were up to 4-folds more sensitive compared to the standard method and showed a potential to reduce the time and volume requirements to run the tests. Such technologies showed a potential opportunity for the acceleration into immunodetection devices with advantages over the 96-well ELISA.

Chapter 4 investigates the implementation of these methods in building sustainable public health actions in Southeast Asia for the prevention and control of infectious diseases. A portable infectious disease diagnostic system that does not require bulky instrumentation or electricity to run was used in the detection of infectious diseases in Southeast Asia. These tools were used in field studies and showed results equivalent to the standard methods with reduced time and volumes needed by 90% less. Such systems were shown to have good potential for use in Southeast Asia and the detection of serologic evidence of human infectious with an emerging virus such as PRV in Central Vietnam highlights the importance of having appropriate detection capacities in place. To support effective public health action in the prevention and control of infectious disease, public health education materials were developed in selected national languages for use during disease outbreaks.

Chapter 5 summarizes the whole thesis. The contributions of this study in sustaining public health action are presented. Future works to build these detection capacities for infectious diseases in Southeast Asia are suggested.