

Thesis progression

Thesis title: Bat virome analysis and development of a platform for assessing the spillover potential of coronaviruses

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1. Introduction

Emerging infectious diseases (EIDs) are an ever-increasing public health risk and economic burden, approximately 75% of EIDs are zoonotic pathogens. (Taylor, L H et al., 2001) Emerging disease outbreaks are initiated by a single transmission or multiple spillover events followed by local human-to-human transmission. Zoonotic spillover can be defined as the cross-species transmission of pathogens from wild animals to humans. The probability of zoonotic spillover is determined by interactions among several factors, including disease dynamics in the reservoir host, pathogen exposure, and the within-human factors that affect susceptibility to infections. Key factors determining spillover potential include cellular and tissue tropism, as well as the virulence and pathogenic characteristics of the pathogen and the capacity of the pathogen to adapt and evolve within a novel host environment. (Escudero-Pérez B et al., 2023)

Bats are important reservoir hosts of many zoonotic viruses that can spillover to infect humans and other domestic or wild mammals. Bats are members of the monophyletic Order Chiroptera and are taxonomically diverse, representing approximately 20% of mammal diversity comprising over 1400 species. They are the only mammals capable of powered flight. They are divided into two suborders: Yinptherochiroptera containing the Pteropodidae (fruit bats) and five families of microbat and Yangochiroptera containing the remaining 14 microbat families. (E.C. Teeling., 2009) There are several zoonotic viruses that spillover from bats to humans including Nipah virus, Hendra virus, Ebola virus, SARS, Middle East respiratory syndrome (MERS), SARS-CoV-2, pandemic avian influenzas, West Nile virus, and Eastern Equine encephalitis virus have emerged from bats. A broad-scale conclusion from metagenomic studies is that bats may be particularly prone to carrying viral families commonly associated with zoonotic disease. Of the more than 16,600 bat-associated viral

sequences on NCBI/GenBank, 30% are the families Coronaviridae. (Kate Van Brussel et al., 2022)

In the past two decades, coronaviruses have been associated with human emergence. The Coronaviruses are subdivided into four genera. The genus Alphacoronavirus (α) contains the human virus HCoV-229E, one other human coronavirus (HCoV-NL63), and many animal viruses. The genus Betacoronavirus (β) includes the prototype mouse hepatitis virus (MHV), the three human viruses HCoV-OC43, SARS-HCoV, and HCoV-HKU1, and the SARS-related coronavirus, Middle Eastern respiratory syndrome (MERS) coronavirus, together with several animal coronaviruses. The genus Gammacoronavirus (γ) contains viruses of cetaceans (whales) and birds, and the genus Deltacoronavirus (δ) contains viruses isolated from pigs and birds. (Burrell CJ et al., 2017) Three major outbreaks of coronaviruses: Severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) caused significant human morbidity and mortality in 2002 and 2012 respectively and, most recently, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused COVID-19 pandemic in 2019 that has caused millions of cases and deaths. (Pustake M et al., 2022) Moreover, most of the virus spillover risk ranking comparison of the top 50 wildlife viruses, including viruses known to be zoonotic and those with unknown zoonotic potential are coronaviruses. (Grange ZL et al., 2021) The associated costs of these preventive efforts would be substantially less than the economic and mortality costs of responding to these pathogens once they have emerged. Thus, efforts to increase preparedness and improve surveillance for emerging coronaviruses therefore represent a priority for global health programs. (Bernstein AS et al., 2022)

Common receptor usage and the ability of viruses to enter and replicate in human cells are major factors linked to spillover potential. To assess the spillover potential of coronaviruses, human proteins or receptors that have potential to support zoonotic spillover (restriction factors, receptors, other cellular proteins) are necessary to identify and determine whether those are few or many. (Escudero-Pérez B et al., 2023)

This study aims to develop a platform for assessing the spillover potential of coronaviruses by investigating common receptor usage of coronaviruses among animal hosts and humans. And analyze the virome profile in bats in Thailand and assess the

spillover potential of identified coronaviruses in bats. This is important for pandemic preparedness and improve surveillance to prevent future coronavirus spillover.

2. Hypothesis

- 2.1. Bat in Thailand may carry coronaviruses.
- 2.2. Coronaviruses identified from bats in Thailand may be capable of spillover to humans.

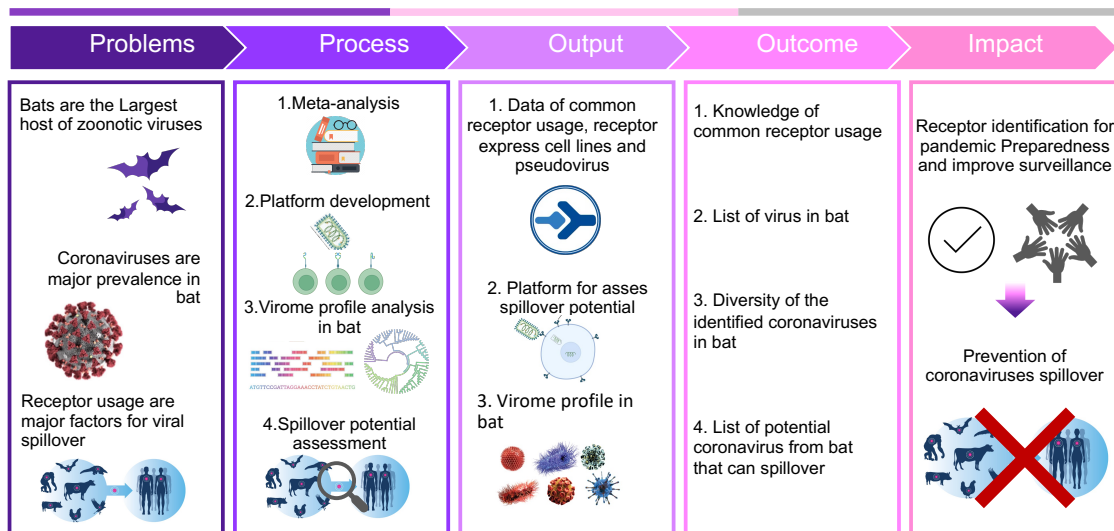
3. Objectives

- 3.1. To develop a platform for assessing the spillover potential of coronaviruses.
 - 3.1.1. To investigate common receptor usage of coronaviruses among animal hosts and humans.
 - 3.1.2. To construct receptor express cell lines and pseudovirus.
- 3.2. To analyze virome profile in bats in Thailand.
- 3.3. To assess the spillover potential of identified coronaviruses in bats.

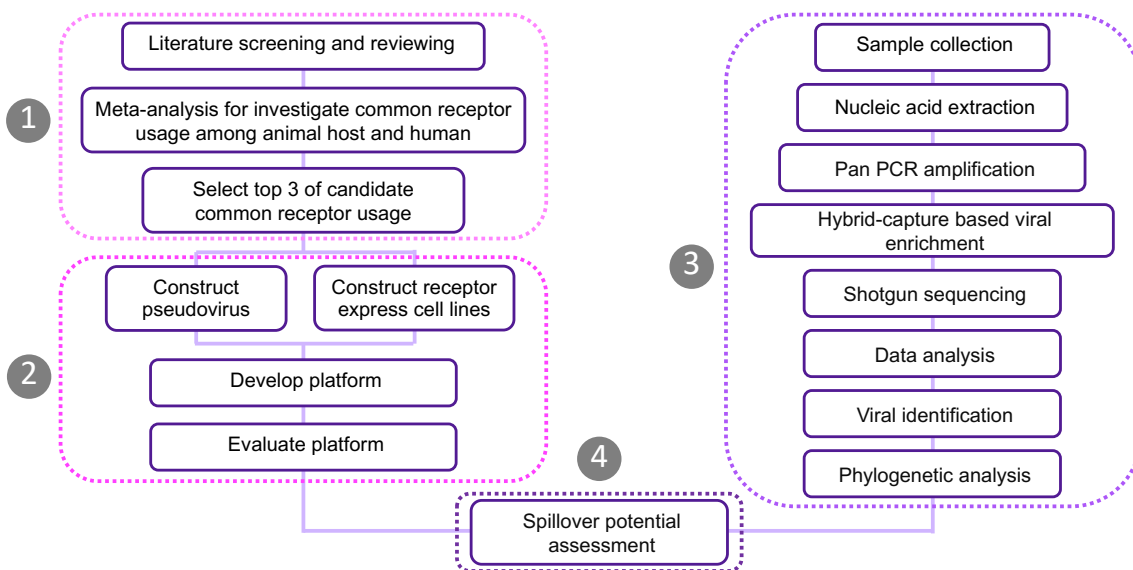
4. Anticipated outcome

- 4.1. Knowledge of common receptor usage of coronaviruses among animal hosts and humans.
- 4.2. List of viruses in bats in Thailand
- 4.3. Diversity of the identified coronaviruses in bats in Thailand
- 4.4. List of potential coronaviruses from bat that can spillover to humans.

5. Conceptual framework



6. Experimental design



8. References

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