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Molecular and virological studies of viruses isolated from bats
(コウモリから単離されたウイルスのゲノムおよびウイルス性状に関する研究)

Emerging infectious diseases (EIDs) pose a significant threat to global public health. Among the most concerning EIDs are those originating from bats, which have been identified as reservoirs for many pathogenic viruses. The emergence of bat-borne diseases is a growing concern. As humans encroach on bat habitats, the risk of disease spillover is likely to increase. In recent decades, scientists have focused on studying viruses in bats that could potentially cause disease in humans. Advancements in technologies such as high-throughput sequencing have aided in the identification of numerous viral sequences from bats.

Among the viruses harbored by bats, the genus *Orthoreovirus* in the family *Reoviridae* are reported. Orthoreovirus (ORV) is a non-enveloped virus with spherical wheel-like structure. Its genome comprises of 10 segments of double-stranded RNA that can be divided into 3 large segments (L1-L3), 3 medium segments (M1-M3), and 4 small segments (S1-S4). ORV is known to cause respiratory and gastrointestinal tract diseases in humans. Currently, three species of ORV have been detected from insectivorous and frugivorous bats, including mammalian orthoreovirus (MRV), Nelson Bay orthoreovirus (NBV), and Broome orthoreovirus.

In this study, virus isolations were conducted from Indonesian fruit bats (IFBs) by reverse transcription polymerase chain reaction (RT-PCR) screening-based and cultured-cell based approaches. To determine ORV infection in IFBs, RdRp gene was screened in RNAs extracted from lung and fecal samples of IFBs by RT-PCR. RdRp genes closely related to NBV were identified in RNA samples extracted from 6 fecal samples of

IFBs collected in Paguyaman. The viruses, which had high nucleotide sequence identity to the NBV genome, were isolated from 5 RT-PCR–positive fecal samples and tentatively designated as Paguyaman orthoreovirus (PgORV). Whole genome analysis of PgORV demonstrated high nucleotide sequence identity with the zoonotic strain, Miyazaki Bali/2007. Phylogenetic analysis suggested the past reassortments of PgORV genome with NBVs isolated from bats and humans in Southeast Asia, indicating circulation of NBVs among bats and humans in this region. PgORV replicated well in human-derived cell lines, and intranasal inoculation of PgORV to mice caused pneumonia with 62.5% mortality rate. Additionally, IFBs showed high seropositivity to PgORV with 81.2%.

To broaden the knowledge on viruses harbored by IFBs, cultured-cell based approach was performed to isolate virus(es) from throat swab, lung, and fecal samples from IFBs. MRVs were isolated from fecal samples collected from *Pteropus vampyrus* in Magelang using mammalian cells which demonstrated cytopathic effect. The isolated MRVs displayed a unique genetic background apart from other known MRVs. Past reassortment events were evidenced in S1 and S4 segments of the isolated MRVs, suggesting cross-species transmission of MRVs among bats, wildlife and humans. *In vitro* characterization of the representative isolated MRV (MRV12-52) showed that the virus efficiently replicated in various cell lines. Furthermore, experimental infection of mice with MRV12-52 caused severe pneumonia with 75% mortality rate.

This study highlight the presence of pathogenic NBV and MRV in IFBs that may potentially related to human diseases in Indonesia. Further study needs to be continued for prevalence of these viruses in humans in Indonesia.