Emerging Pteropine orthoreoviruses and their potential impact on public health

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Letter to the editor

Emerging *Pteropine* orthoreoviruses and their potential impact on public health

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Abstract:

A group of viruses, collectively known as *Pteropine*orthoreoviruses (PRVs), have recently been found in fruit bats and humans in Southeast Asia, Australia, and some African countries. This article intends to briefly discuss what is known about these viruses and their potential significance in public health and to advocate for increased surveillance of these zoonotic viruses to prevent potential future disease outbreaks, as well as to highlight a recent publication on this topic that was selected as an editor's choice article in the*Journal of Medical Virology* [1].

Body of texts

Flying foxes and bats that belong to the *Pteropus* genus have been known to be reservoirs for many different viruses, including orthoreoviruses. Orthoreoviruses belong to the *Reoviridae* family and are known for their ability to infect many mammalian species, including humans. These so-called *Pteropine* orthoreoviruses (PRVs) are named after their reservoir's genus[2]. The first PRV isolate was discovered in bats in 1968 and was named the Nelson Bay virus for the locale (Nelson Bay in Southeastern Australia) where it was discovered[3]. Since then, many PRVs have been discovered in bats and humans in different parts of the world, except for those in North and South America (Figure 1), and most of the recent strains of this virus are genetically related to the original isolate.

Like other reoviruses, the PRV genome consists of 10 double-stranded RNA segments (S1-S4, M1-M3, and L1-L3). The segmented genomes allow the virus to evolve as they increase the potential for genome reassortment, in which the segmented genome from one strain can exchange with the segmented genome of another, and thus, enhancing the genetic diversity of the progeny virus. These genomic exchanges can allow the new virus to select for more efficient mechanisms of viral entry, genome replication, immune evasion, and/or expansion of the host range for the infection[4]. This particular viral lifestyle can increase inter- and intraspecies transmission events, making these viruses more adaptable to different host species and more prone to cause disease outbreaks[5-9].

Out of the seventeen (17) currently known PRV strains (Table 1), eight (8) have been isolated from bats, one (1) has been isolated from non-human primates and another eight (8) have been isolated from humans who either live in areas where these PRVs are endemic or from travelers to endemic areas. Some of the human cases have resulted from either direct contact with the infected fruit bats or human-to-human transmission events. PRV often causes flu-like symptoms, and for this reason, it is either not being diagnosed immediately or is often being misdiagnosed. Also, most of the currently available clinical respiratory diagnostic assays do not include PRV as a potential candidate, which can lead to undiagnosed patients[5,6]. In severe cases, PRV infection can lead to acute respiratory distress syndrome, the mechanism of which is unknown[10-12].

A recent article published in the *Journal of Medical Virology* [1] looked at the role of PRV as a causative agent for acute respiratory infections (ARI) in humans. In this article, the authors selected patients who were being seen at the primary care clinics in Kuala Lumpur, Malaysia from March 2012 to May 2014 for ARI-related symptoms. A total of 3,935 nasal swab samples were collected and tested using the xTAG Respiratory Viral Panel FAST assay, which can detect fifteen different respiratory viruses. Forty-nine percent (49%) of those samples were negative for any known respiratory viruses. When 632 of those samples were then tested for PRVs, 14 (2.2%) of them were positive for these viruses. The authors also reported higher PRV-positive incidences in their patients in August of 2013 (13.3%) and April and May of 2014 (20% and 33.3%, respectively). Additionally, they were able to sequence the new PRV genomic segments that showed a new reassortant strain (PRV18UM), which consists of the segmented genomes from both the Melaka and Kampar virus strains. They used this new strain of the virus to assess its replication kinetics in human cardiomyocyte cell line (AC16), African green-monkey cell line (Vero), and human oral keratinocytes and nasopharyngeal epithelial cell lines (OKF-6 and NP69). Even though this new strain of the virus replicated slower in the OKF-6 and NP69 cells than in the AC16 and Vero cells, it was shown for the first time to be able to replicate in human head and neck cells. Interestingly, the authors also observed that the S segments from most PRV strains isolated from humans in their cohort were a mixture of the viral genomic segments from both non-human primate and bat strains, which strongly suggests this as a mechanism of cross-species transmissions among three different mammalian species, among other genetic diversification mechanisms observed.

This editor's choice article[1] reports the first PRV surveillance effort in urban areas, which suggests that PRVs are more prevalent in populated areas than have previously been presumed. As PRVs are zoonotic viruses, people who are living and/or working in densely populated areas or in congregate settings (e.g., airports, hospitals, nursing homes, childcare centers, schools, indoor sporting and other entertainment facilities, restaurants, jails, prisons, shelters, residential living facilities, etc.) and those who are living in rural areas and/or are more likely to be exposed to fruit bats need to be more aware of the potential exposure

to these emerging viruses. Public health officials in endemic regions also need to consider conducting routine surveillance for these emerging viruses to prevent potential future disease outbreaks caused by these *Pteropine* orthoreoviruses (PRVs).

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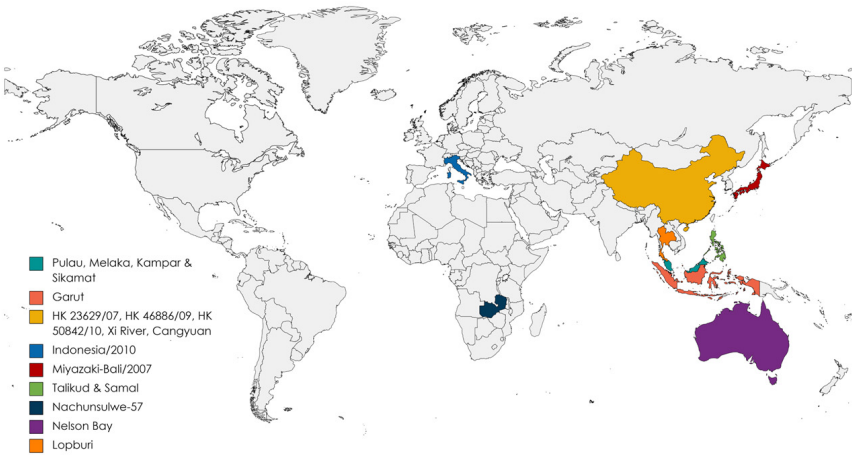
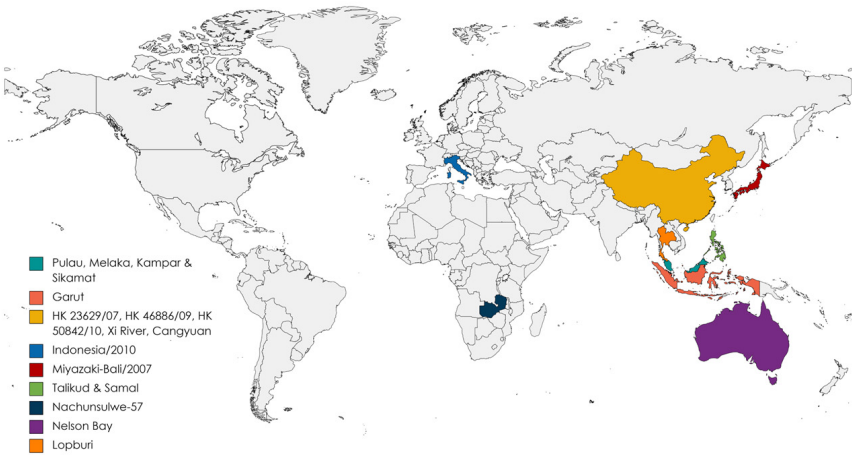


Figure 1: World map of the countries where *Pteropine*orthoreoviruses have been found.

Table 1: Known *Pteropine* orthoreoviruses

Virus	**Year Isolated**	**Host**	**Location (Imported Country)**
Nelson Bay	1968	Bat	Australia
Pulau	1999	Bat	Malaysia
Melaka	2006	Human	Malaysia
Kampar	2006	Human	Malaysia
HK23629/07	2007	Human	Hong Kong (Indonesia)
Miyazaki-Bali/2007	2007	Human	Indonesia (Japan)
HK46886/09	2009	Human	Hong Kong (Indonesia)
HK50842/10	2010	Human	Hong Kong (Indonesia)
Sikamat	2010	Human	Malaysia
Xi River	2010	Bat	China
Indonesia/2010	2010	Bat	Indonesia (Italy)
Cangyuan	2013	Bat	China
Lopburi	2013	Non-human primate	Thailand
Talikud	2013	Bat	Philippines
Samal	2013	Bat	Philippines
Garut	2016	Bat	Indonesia
Nachunsulwe-57	2017	Bats	Zambia



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