# FRUIT BATS AS NATURAL RESERVOIR OF HIGHLY PATHOGENIC HENIPAVIRUSES: HIGH PERMISSIVENESS OF REPROGRAMMED PTEROPUS BAT CELLS

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# Abstract Submission

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## FRUIT BATS AS NATURAL RESERVOIR OF HIGHLY PATHOGENIC HENIPAVIRUSES: HIGH PERMISSIVENESS OF REPROGRAMMED PTEROPUS BAT CELLS

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**Abstract:** Bats are asymptomatic hosts for numerous viruses, including highly pathogenic zoonotic henipaviruses, Nipah (NiV) and Hendra. Understanding of how bats control viral infection requires better characterization of bat-derived viruses and development of relevant permissive cellular models. We analysed NiV isolate obtained from a *Pteropus lylei* bat in Cambodia in 2003 (CSUR381), where human outbreaks of NiV infection have not been detected so far. Full-genome sequencing and phylogenetic analyses confirmed that CSUR381 is part of the NiV-Malaysia genotype. Cell permissiveness was similar in both bat and human cell lines and replication of CSUR381 was alike to other two NiV isolates. In the hamster animal model CSUR381 induced lethal infection. These data suggest that the Cambodia bat-derived NiV isolate has high pathogenic potential, providing an insight for better risk assessment for future NiV outbreaks in Southeast Asia. Most of the available bat cells are immortalized lines, significantly impacting the overall cell response that may alter the virus-cell interactions. Therefore, by applying a somatic reprogramming protocol to *Pteropus* bat primary cells, using a novel combination of ESRRB, CDX2 and c-MYC transcription factors, we generated bat reprogrammed cells exhibiting neural stem cell-like characteristics. These cells present a unique interferon-stimulated transcriptomic signature but still produce and respond to IFN type I. In contrast to primary bat cells, these reprogrammed cells are highly susceptible to infection by *Henipavirus*, even more than Vero cells, commonly used for virus isolation. Future direct reprogramming of bat primary cells into various differentiated cell types should facilitate the isolation of new bat viruses and further studies of virus-bat interaction, towards better understating of the efficient bat anti-viral response.