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Immune Bats & Viral Spillovers: The Ultimate Pandemic Threat?

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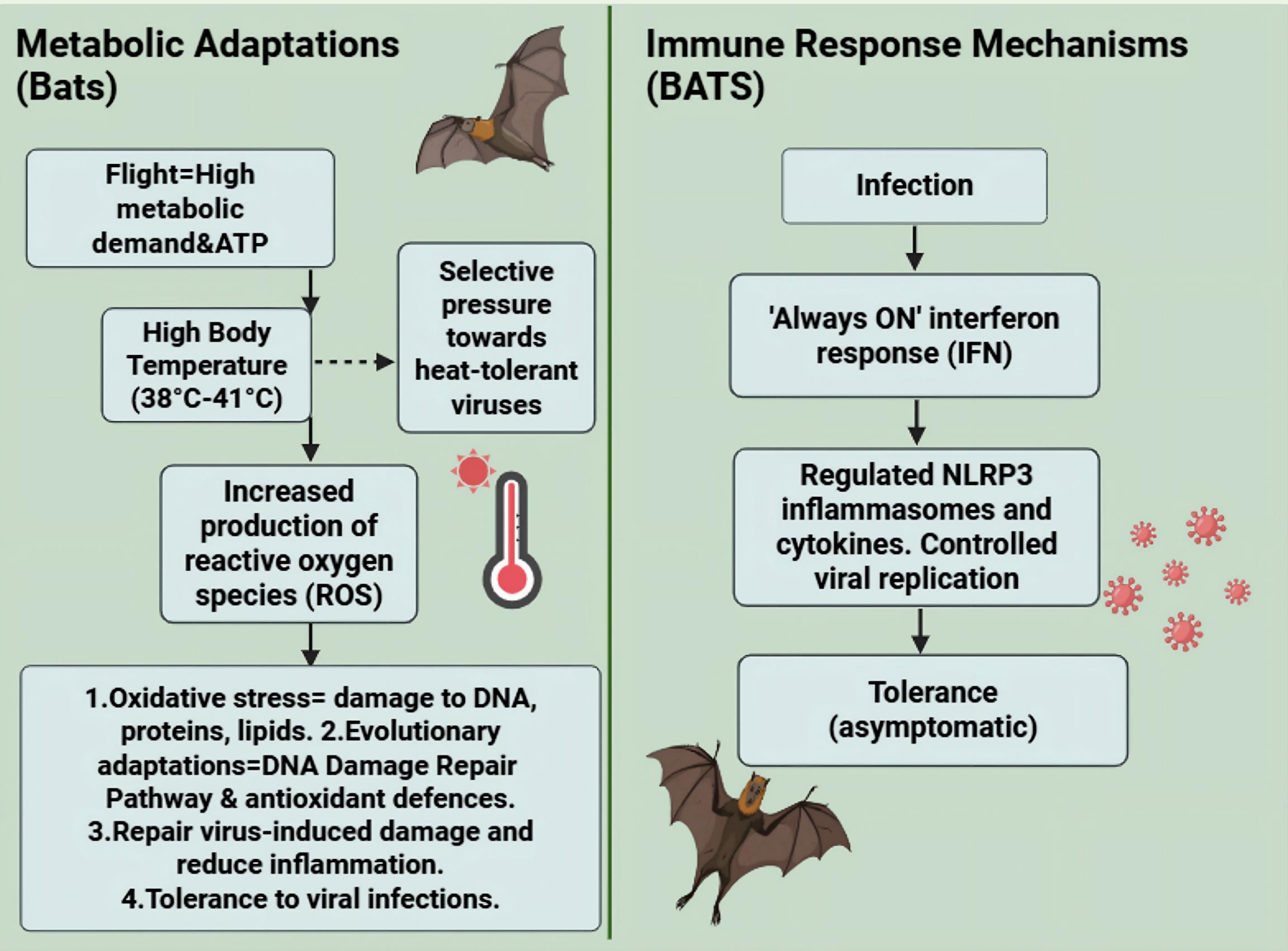
1.Abstract

- Bats act as asymptomatic reservoirs for highly pathogenic viruses, including Nipah virus (NiV) and Ebola virus (EBOV).
- This project analyses the evolutionary adaptations enabling bat viral tolerance and compares the molecular pathways of NiV and EBOV to evaluate their pandemic potentials and proposes a ferret-model study to identify respiratory mutations in NiV, aiming to prevent future pandemics.

2.Introduction

- Zoonotic bat viruses are a growing global threat due to habitat loss and spillover to humans.
- While EBOV causes regional endemics, NiV is a high-priority pathogen with up to 70% fatality rate and respiratory spread potential[1].

3.Viral Tolerance in Bats



Metabolic Adaptations (Bats)

Flight=High metabolic demand&ATP

High Body Temperature (38°C-41°C)

Selective pressure towards heat-tolerant viruses

Increased production of reactive oxygen species (ROS)

1.Oxidative stress= damage to DNA, proteins, lipids. 2.Evolutionary adaptations=DNA Damage Repair Pathway & antioxidant defences. 3.Repair virus-induced damage and reduce inflammation. 4.Tolerance to viral infections.

Immune Response Mechanisms (BATS)

Infection

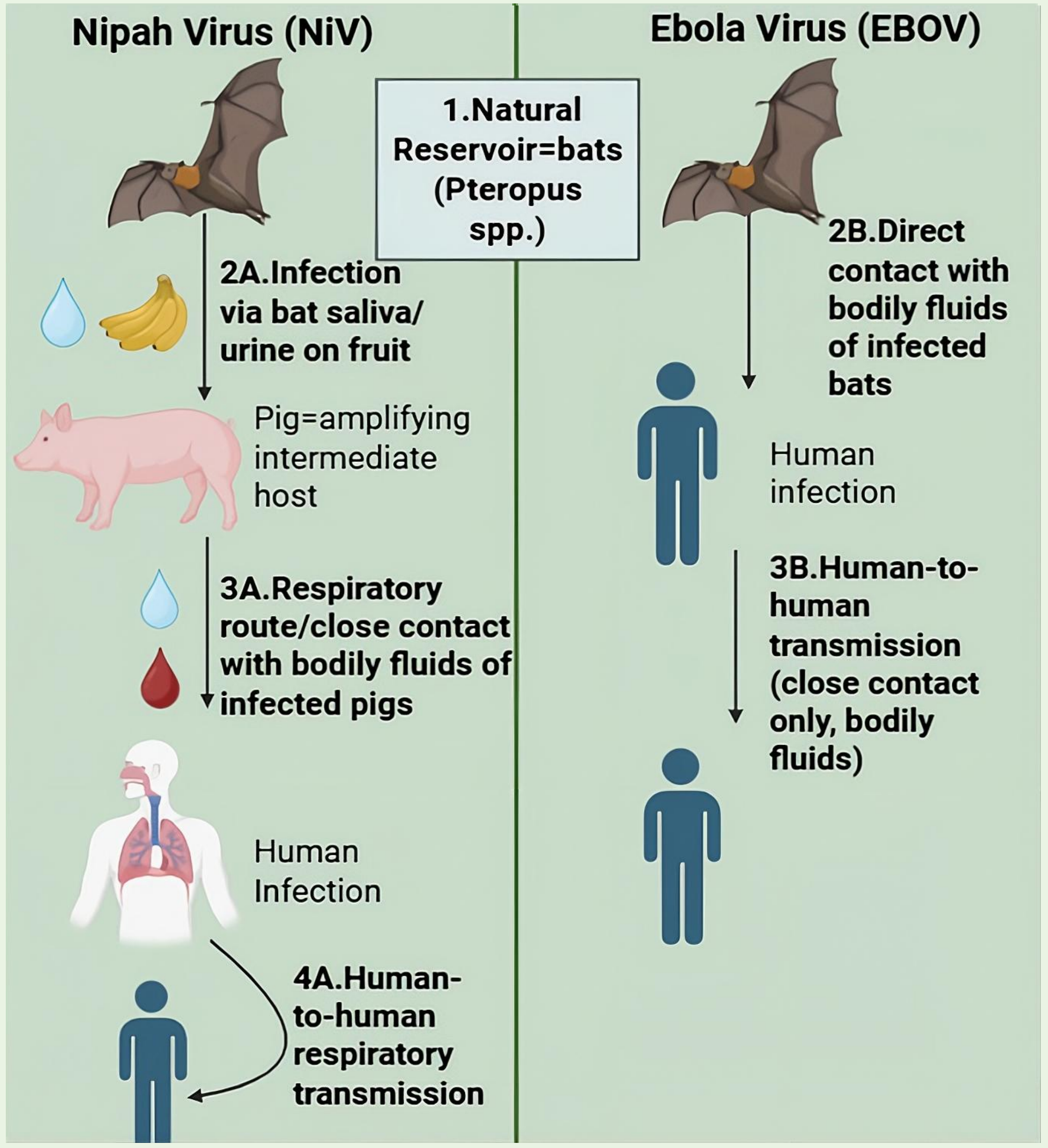
'Always ON' interferon response (IFN)

Regulated NLRP3 inflammasomes and cytokines. Controlled viral replication

Tolerance (asymptomatic)

- 'Flight as Fever'- flight metabolism raises bat temperatures up to 41°C, naturally selecting for heat-tolerant viruses. These viruses are stable against human inflammation.
- DNA Damage Repair Pathway and antioxidant defenses.
- 'Always ON Immunity'- bats constantly express IFN-α. This controls viruses without triggering the fatal hyperinflammation seen in humans.

4.Evaluating the Pandemic Threat: NiV vs. EBOV



Nipah Virus (NiV)

Ebola Virus (EBOV)

1.Natural Reservoir=bats (Pteropus spp.)

2A.Infection via bat saliva/ urine on fruit

Pig=amplifying intermediate host

3A.Respiratory route/close contact with bodily fluids of infected pigs

Human Infection

4A.Human-to-human respiratory transmission

2B.Direct contact with bodily fluids of infected bats

Human infection

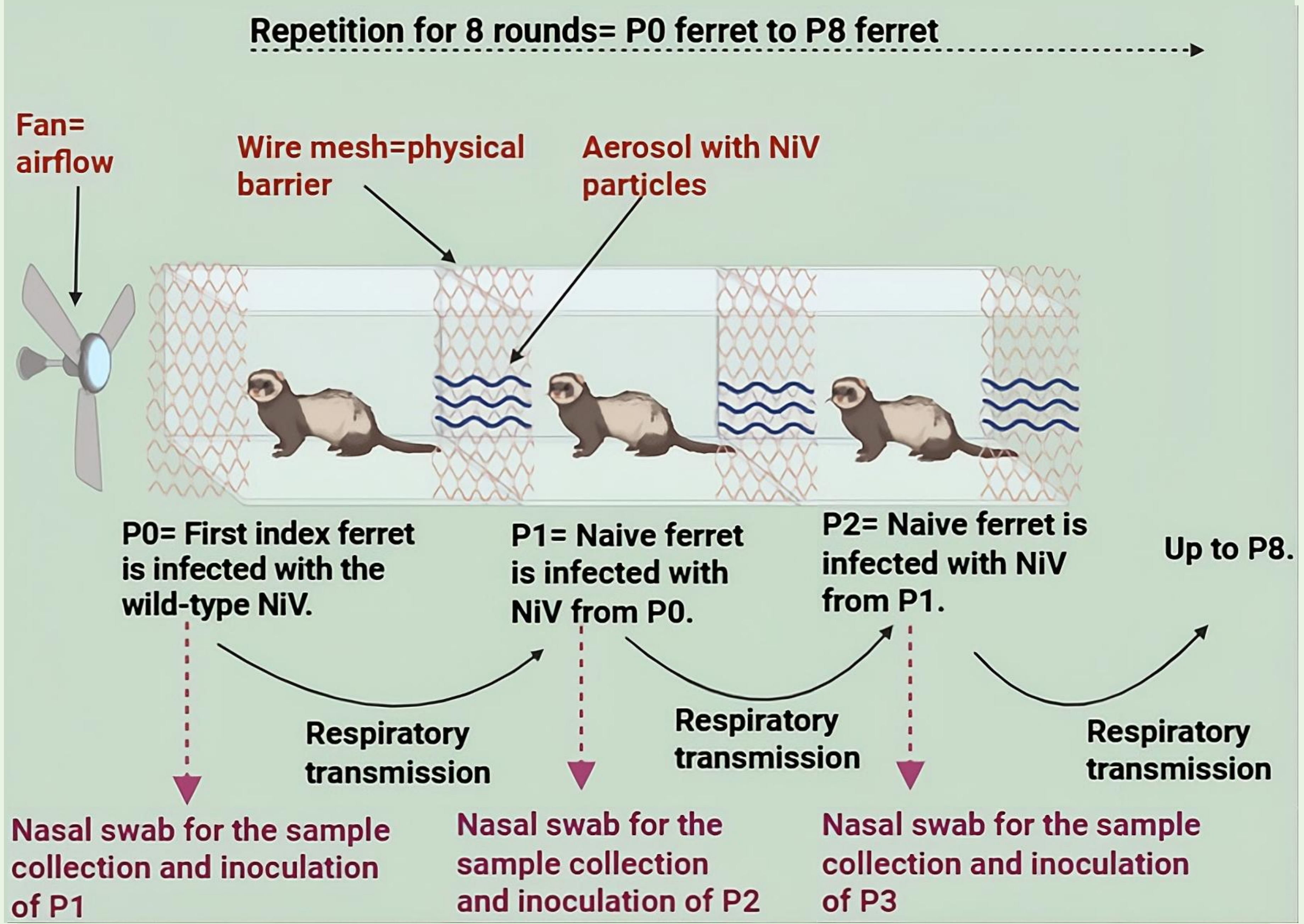
3B.Human-to-human transmission (close contact only, bodily fluids)

NiV vs. EBOV Transmission

Feature	NiV	EBOV
Cellular Receptor	Ephrin-B2/3 (Broad tropism)[2]	NPC1 (via GP cleavage)
Transmission Route	Respiratory droplets, contaminated food, and intermediate hosts (pigs)	Direct contact with infected bodily fluids/ secretions
Pandemic Potential	High (Due to respiratory capability and human-to-human spread)	Low / Regional (Restricted by contact-dependent transmission)[3]

5.Anticipating NiV Mutations

- We lack data on which specific NiV mutations enable efficient human respiratory spread.
- Method= 8 rounds of *in vivo* serial passage using ferrets (physically separated by wire mesh to isolate aerosol transmission)[4].
- Reverse genetics will be used to synthesise and confirm the high-risk nature of the identified mutations.



Repetition for 8 rounds= P0 ferret to P8 ferret

Fan= airflow

Wire mesh=physical barrier

Aerosol with NiV particles

P0= First index ferret is infected with the wild-type NiV.

P1= Naive ferret is infected with NiV from P0.

P2= Naive ferret is infected with NiV from P1.

Up to P8.

Respiratory transmission

Respiratory transmission

Respiratory transmission

Nasal swab for the sample collection and inoculation of P1

Nasal swab for the sample collection and inoculation of P2

Nasal swab for the sample collection and inoculation of P3

6.Conclusion

- NiV's respiratory capacity makes it a significantly higher global threat than EBOV.
- Proactively identifying airborne mutations before they emerge naturally enables targeted surveillance and proactive antiviral design.

7.Acknowledgements

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8.References

1. Sun, B., et al., 2018. Phylogeography, Transmission, and Viral Proteins of Nipah Virus. Virologica Sinica. 33(5), pp.385–393.
2. Negrete, O.A., et al., 2005. EphrinB2 is the entry receptor for Nipah virus, an emergent deadly paramyxovirus. Nature. 436(7049), pp.401–405.
3. Vetter, P., et al., 2016. Ebola Virus Shedding and Transmission: Review of Current Evidence. Journal of Infectious Diseases. 214(suppl 3), pp.177–184.
4. Rockx, B. and Mire, C.E. 2023. Ferret Models for Henipavirus Infection. Methods in molecular biology. 2682, pp.205–217.
5. The figures were created using BioRender.com.

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