Countering Nipah Virus: A Review of Pathogenesis, Countermeasure Design, and Biosecurity Challenges

Levi Woon

Abstract

Nipah virus (NiV) is a zoonotic pathogen classified by the World Health Organization as a priority pathogen with epidemic potential. Driven by distinct viral lineages in Malaysia and Bangladesh, this pathogen can induce severe respiratory illness and lethal encephalitis, with human mortality rates ranging from ~40% to ~75% across outbreak zones, depending on the strain. This review paper focuses on the zoonotic origins and molecular mechanisms underlying NiV infection while highlighting both current medical countermeasures and emerging translational avenues to counter NiV's capacity for host immune evasion. By mapping out how these novel therapeutic strategies target the host-pathogen interface, we aim to inspire future countermeasure development and improve clinical outcomes for this biosecurity-relevant disease.

Overview of Nipah Virus

Nipah virus (NiV) is an extremely pathogenic, zoonotic, single stranded RNA virus. Zoonotic viruses are viruses commonly transmitted to humans through animals. The pathogen exists in an animal reservoir where it can stay without dying out, eventually spreading to humans through infected animals or contaminated materials like food or fluids. Nipah virus is part of the family *Paramyxoviridae*, which is a family of enveloped, non-segmented, negative sense single stranded RNA viruses (Madhukalya et al., 2025). Members of the family will usually infect many mammals and birds, causing damage to the respiratory and nervous system. Viruses of the *Paramyxoviridae* family can range from common viruses like the measles virus and mumps virus all the way to lethal viruses such as Nipah virus (Madhukalya et al., 2025). Within that family, Nipah virus belongs to genus *Henipavirus*, a smaller group within the family that shares more commonalities. Members of genus *Henipavirus* tend to infect several different mammal species, are highly pathogenic, and can harbor a large number of hosts (Madhukalya et al., 2025). The most common hosts for viruses in this genus are fruit bats of genus Pteropus (Madhukalya et al., 2025). Hendra virus, a member of genus *Henipavirus*, is the closest relative to Nipah virus, and shares many commonalities, such as the same host and similar tissue tropism (Madhukalya et al., 2025). These similarities have led to attempts to utilize studies on Hendra in regards to finding antivirals and treatments for Nipah virus.

Nipah virus contains a single stranded RNA genome, meaning genetic material is stored in RNA rather than DNA (Pellett et al., 2014). Single stranded means that the virus consists of only one RNA strand as opposed to the complementary strands of DNA (Pellett et al., 2014). However, this single strand means that Nipah, along with other RNA viruses, can mutate very fast, as RNA replication tends to be less accurate than DNA replication, allowing for more mutations to survive the replication process and pass their traits down (Madhukalya et al., 2025). In addition to being single stranded, Nipah virus is also negative-sense. This means that the virus cannot be used immediately to make proteins with the cell’s organelles (Madhukalya et al., 2025). The RNA genetic sequence is already complementary to typical mRNA that can be translated into protein, so the virus must make a positive sense strand of RNA before protein production can begin (Pellett et al., 2014). This is done with RNA-dependent RNA polymerase

(RdRp), an enzyme coming from the virus itself. Since humans do not possess an enzyme to copy RNA, this enzyme is used and brought by viruses in order to begin RNA synthesis (Pellett et al., 2014). Finally, the virus consists of non-segmented genomes, meaning that Nipah virus contains one continuous RNA molecule that contains all of its genetic material. This genetic material contains the genes for encoding proteins for the virus, with 6 main proteins existing (Madhukalya et al., 2025). The N protein, or nucleocapsid protein, is used to protect the RNA genome. The P protein, or phosphoprotein, helps regulate polymerase activity. The M protein, also known as the matrix protein, helps with the assembly of new viral particles. The F and G proteins (Fusion protein and attachment glycoprotein) help with membrane attachment and infiltration. Finally, the L protein, also called the large polymerase protein, forms the RdRp (Madhukalya et al., 2025).

The infectious Nipah viral particle, or virion, consists of several components. The virion is the particle that exists outside of a host cell. It contains all the genetic material and proteins needed to protect the virus and to infect healthy cells (Pellett et al., 2014). The virus itself is an enveloped virus, meaning it is protected by a lipid membrane (Madhukalya et al., 2025). This membrane is attained when new viruses bud from infected cells, taking the cell's membrane with them as their own (Madhukalya et al., 2025). Although this enveloped trait can help fusion with host cells, it can be unstable due to lipid membranes. During its lifespan, Nipah virus uses several different proteins to aid the life cycle, reproduction, and production of Nipah virus (Figure 1). The N protein wraps around the RNA genome, making the nucleocapsid itself, which protects the genome. The M protein is found in between the nucleocapsid and envelope, which provides structural support. It also can assist with the assembly and export of new virus particles. The G and F proteins work together to aid Nipah virus in fusion and infection. The G protein, protruding from the virus, binds to a cell’s ephrin-B2 and ephrin-B3 receptors. Upon attachment, the F protein activates and brings the virus envelopes and host cell membrane together, causing them to fuse and thus allowing the RNA genome to initiate infection upon entry (Madhukalya et al., 2025).

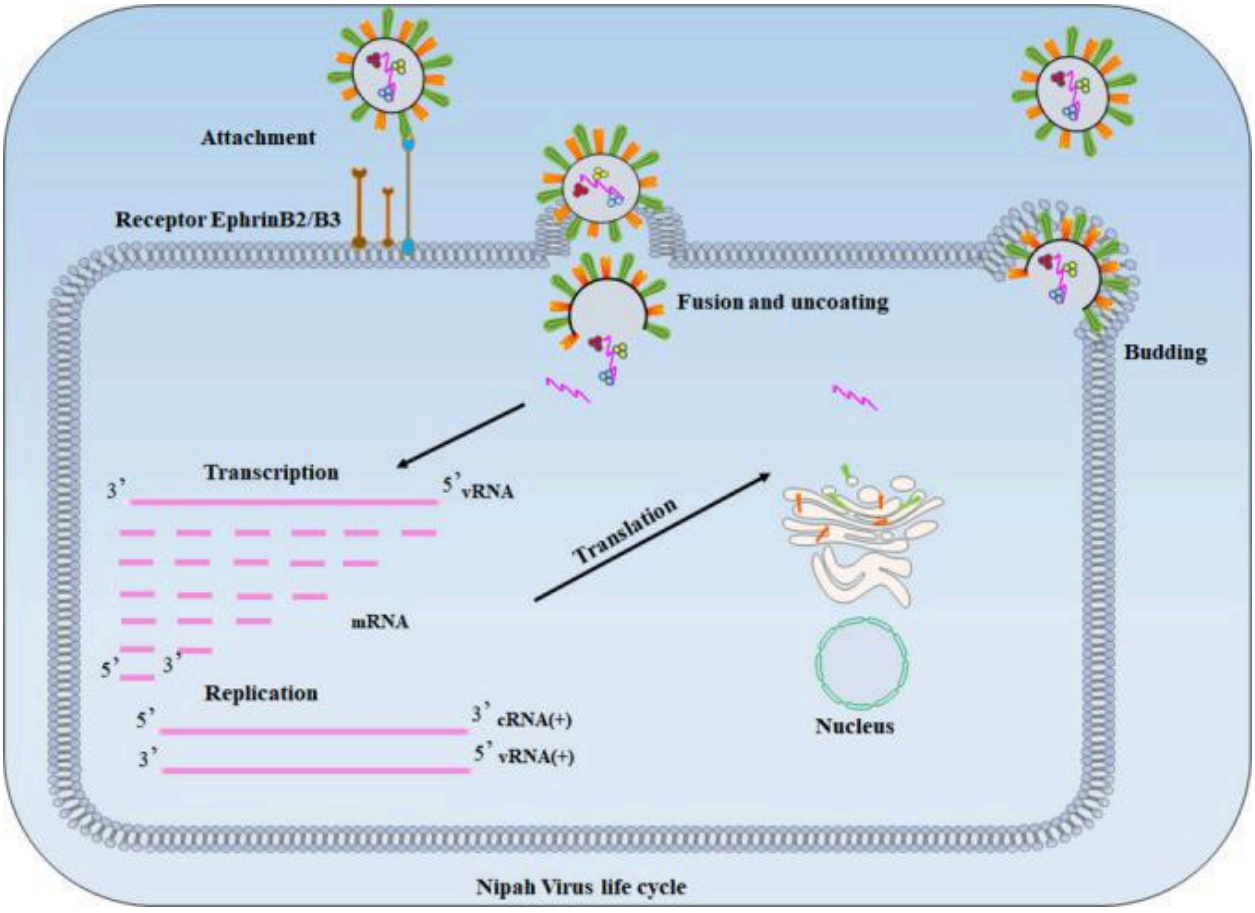


Figure 1. Infection method of Nipah virus. Adapted from Madhukalya et al., 2025 [1] under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Epidemiology

The first documented accounts of Nipah virus came from a small Malaysian town in 1998 (Madhukalya et al., 2025). It then was documented spreading to Singapore via infected pigs as a host. Since then, Nipah virus outbreaks have frequently arisen in Bangladesh and India. Since the natural hosts of the *Pteropus* fruit bats reside in South and Southeast Asia, most outbreaks are confined to that region. Anything extending past the geographic habitat of the *Pteropus* fruit bats usually experiences fewer outbreaks, if any, while most areas within their domain experience outbreaks of the virus (Madhukalya et al., 2025). Spillover can happen from the farming and harvesting of contaminated date palm sap, or distribution of food containing water contaminated with bat saliva. These human agricultural and environmental interactions are one of the main forms of human infection (Madhukalya et al., 2025).

In zoonotic transmission, there are generally two kinds of hosts: Reservoir hosts and intermediate hosts. Reservoir hosts coexist with the virus, not being affected by it while letting it reside within them, the reservoir host of Nipah virus being the *Pteropus* fruit bat species. The intermediate host is an animal that has been infected by the reservoir host and can still infect humans (Madhukalya et al., 2025). There are two main major strains of Nipah virus: NiV-B and

NiV-M. NiV-B is dominant in Bangladesh and India, with the reservoir host being *Pteropus medius*. NiV-M is dominant in Malaysia, with the reservoir host being *Pteropus hypomelanus*. Additionally, NiV-M has an intermediate host in pigs. After being exposed to fruit contaminated by *Pteropus hypomelanus*, they become infected and spread the virus while it grows in numbers (Madhukalya et al., 2025). The largest Malaysian outbreak was spread through close contact with infected pigs. Horses have also been noted as an intermediate host in a recent Philippines outbreak (Madhukalya et al., 2025).

There are various transmission mechanisms that lead to humans becoming infected with Nipah virus (Figure 2). The first one is directly from the *Pteropus* fruit bats to humans. The virus can be transmitted if a human ingests anything contaminated with bat saliva or urine, additionally spreading through contaminated date palm sap (Madhukalya et al., 2025). Another transmission path is from bats to pigs to humans. Pigs will become infected in a similar way, and they will spread the disease through contaminated urine or waste, which workers at slaughterhouses and farms can come in close contact with. Finally, human to human is a transmission mechanism most common in NiV-B, which is spread through respiratory fluids, close family contact, and transmission at hospitals. Some NiV-B outbreaks have reported a 33-75% human transmission rate (Madhukalya et al., 2025).

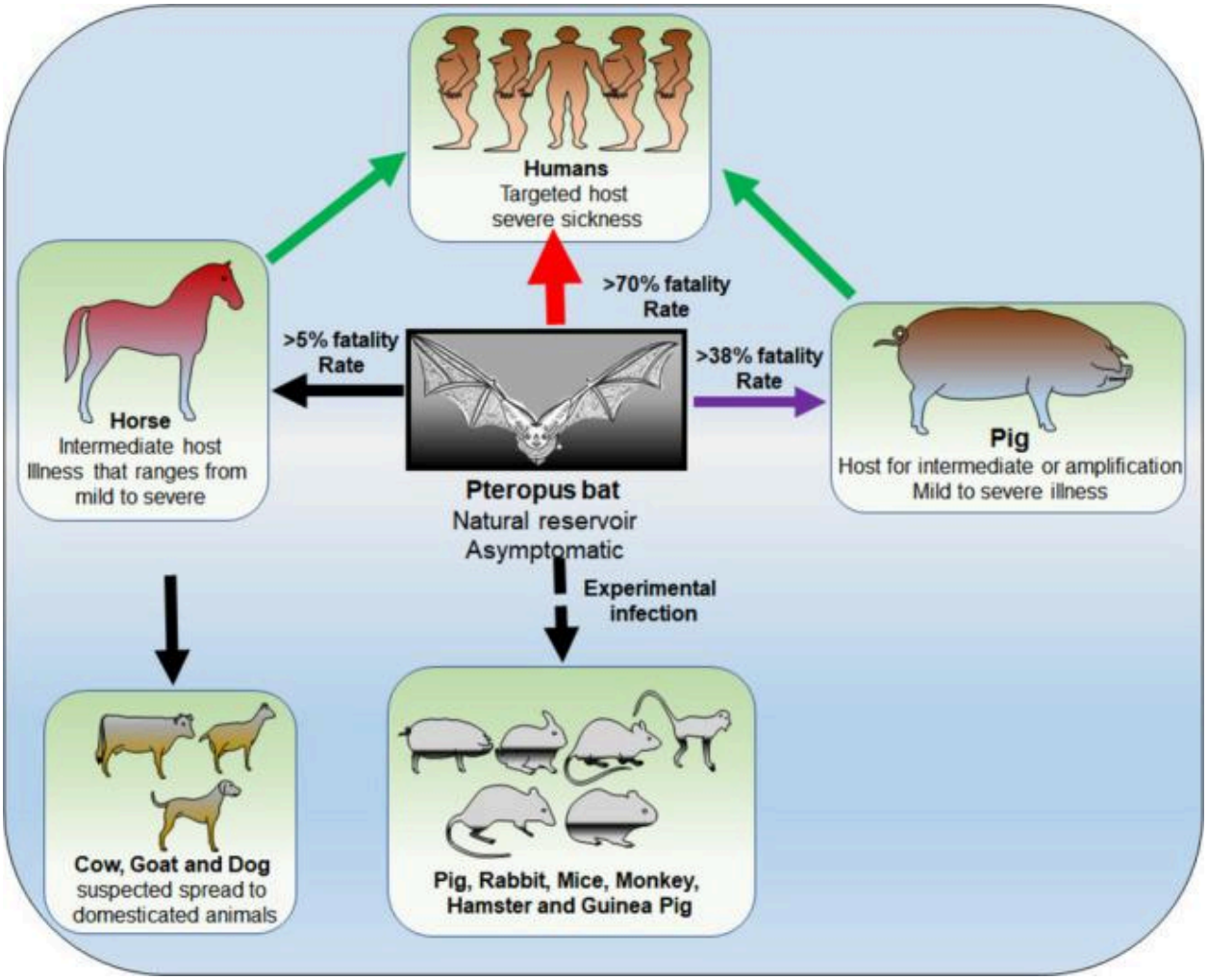


Figure 2. Various hosts of Nipah virus. Adapted from Madhukalya et al., 2025 [2] under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

The molecular basis of NiV transmission shows how and why the virus is so concerning for international health organizations. Initially, the G glycoprotein will bind to ephrin-B2 and ephrin-B3 receptors on cells, subsequently leading the F glycoprotein to begin cell membrane fusion, allowing the virion to put its genetic material and necessary proteins within a now infected cell (Madhukalya et al., 2025). Once viral RNA enters the cell, replication begins and the virus begins to spread. Ephrin-B2 and ephrin-B3 receptors are found in high quantities across microvascular endothelial cells, neurons and respiratory epithelial cells, which is why Nipah virus mainly infects the brain, lungs, and blood vessels (Madhukalya et al., 2025).

The clinical progression of Nipah virus is another reason for alarm. The virus typically incubates for 4-14 days, and causes early symptoms of fever, headache, and fatigue. It can then progress to respiratory issues such as coughing, pneumonia, and respiratory distress (Madhukalya et al., 2025). Following that, neural symptoms begin to show, such as encephalitis, seizures, and an altered consciousness. After that, the viral infection can progress to a coma and later even death. NiV-M tends to be more of a neurological infection, with a lower mortality at around 40% (Madhukalya et al., 2025). NiV-B is more respiratory, with greater human-to-human transmission and a higher mortality at around 75% (Madhukalya et al., 2025).

Current Treatments

The pathogenesis of Nipah virus has caused much worry, especially as there are no currently clinically approved Nipah-specific treatments or cures (Madhukalya et al., 2025). Once the virus has entered the body through the respiratory tract or mucous membrane, it undergoes its fusion process utilizing its F and G glycoproteins. It then inserts viral RNA into the cell, and replication begins as the virus spreads from cell to cell. One method in which Nipah virus utilizes is syncytia, where cells will merge and fuse together into a mass of cells to allow the virus to spread without ever exiting the original infected cell (Madhukalya et al., 2025). This allows the virus to avoid antibodies easier, as it does not need to exit the cell to infect other cells. When NiV infects endothelial cells, it causes vasculitis and leads to vascular damage. After spreading to the lungs and central nervous system (CNS), respiratory distress and encephalitis follow (Madhukalya et al., 2025).

Since no clinically approved NiV-specific treatments exist, care and assistance are purely supportive and management based. Things such as oxygen therapy, mechanical ventilation, intensive care monitoring, and managing brain swelling are all tools used to help manage the damage that Nipah virus causes. However, several antiviral drugs created for other viruses have been researched and studied in laboratories and animal studies. One example is Remdesivir, an antiviral that targets the RdRp and aims to prevent viral RNA synthesis, thus reducing viral replication (Madhukalya et al., 2025). Studies with African green monkeys have shown a 100% survival rate in experimental conditions and provides a promising start for the antiviral, currently undergoing further investigation before submitting for approval (Madhukalya et al., 2025). Another antiviral is Ribavirin, a drug intended to interfere with RNA synthesis by attaching to the

RNA polymerase and preventing efficient replication (Madhukalya et al., 2025). It has been associated with reduced mortality in humans, but has shown mixed results in animal studies. Additionally, side effects like anemia and nausea have occurred, causing researchers to remain cautious about Ribavirin as an approved drug (Madhukalya et al., 2025). Favipiravir has also been studied recently as a potential drug to use. Favipiravir works as another RNA Polymerase inhibitor, and has proven to be heavily effective against Syrian hamsters and reduced mortality amongst the hamsters, proving to be promising for human treatment (Madhukalya et al., 2025). All these drugs, along with several others, are currently being tested and researched in an attempt to combat the growing threat of Nipah virus. In addition to these antiviral drugs, several new fields are being researched to create new ways to fight Nipah virus and other viruses alike.

Emerging Treatments

AI and Machine Learning

Currently, developing and testing drugs through traditional drug discovery is expensive and time consuming. Due to the fact that NiV outbreaks are unpredictable, conventionally finding new drugs to combat the sporadic virus is a difficult challenge. Researchers have begun utilizing AI and machine learning to accelerate the drug testing and discovery process. Various AI programs can screen several thousands, even millions of chemical compounds to determine what compounds are worth testing. There are two main types of drugs that are being tested with these methods: small-molecule drugs and peptide drugs (Figure 3). Small-molecule drugs work by targeting specific-shaped binding sites on selected proteins, while peptide drugs operate by filling deep, specialized pockets or binding sites on “undruggable targets.” Peptide drugs can also interfere with protein-protein interactions (PPI), interfering how various proteins would interact with each other, binding being an example. Machine learning can also be utilized to predict what molecules can bind to the viral proteins, and a molecular docking simulation (such as AutoDock Vina) can estimate if the compound will fit well in the bonding site of the viral protein (Lin et al., 2026). AI and machine learning can then simulate whether the molecule will remain stable over time (using programs like GROMACS), and if it presents any inherent health issues such as toxicity or lack of solubility (Lin et al., 2026).

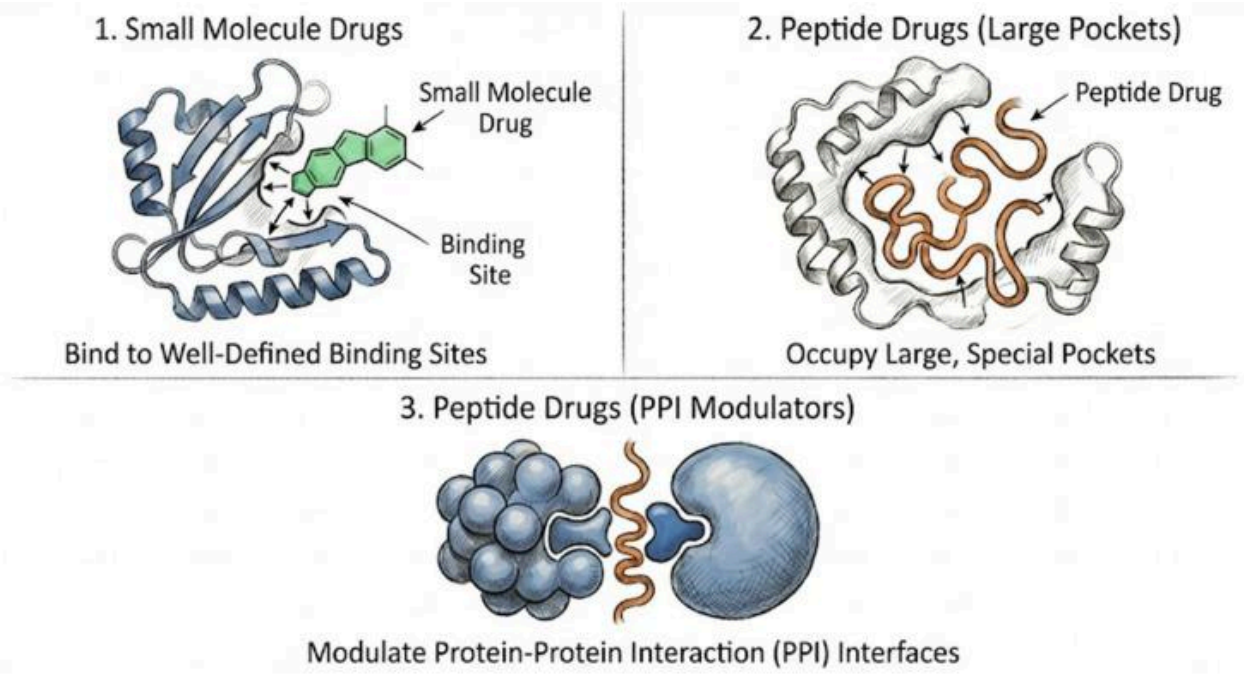


Figure 3. Various types and purposes of drugs. Reproduced from Lin et al., 2026 [3] under the terms of the Creative Commons Attribution 4.0 International License.

In NiV specifically, AI and machine learning have been used to simulate the production and implementation of antiviral drugs on a few specific viral targets, namely the G glycoprotein, F glycoprotein, and the N protein. In a recent study, AI and machine learning were used to screen compounds that could be used against the aforementioned NiV proteins (Randhawa et al., 2022). It was found that the phytochemicals RASE0125 and CARS0358 were the compounds with the best predicted interactions (Randhawa et al., 2022). Both phytochemicals were theorized to be capable of interacting with multiple viral proteins. Phytochemicals are natural inhibitors found in plants, which have shown to boost a plant's defenses against viruses such as SARS-CoV-2 and Zika. In interacting with multiple proteins, these chemicals can inhibit several stages of the virus, ensuring that no viral process can continue. Specifically binding to the G, F, and N proteins can prevent the binding, fusion, and replication of Nipah, preventing further spread or infection if successful (Randhawa et al., 2022). Finding a compound that targets all 3 of these proteins is especially useful because it allows for studies to focus on the development and administration of one specific antiviral, rather than a combination of multiple. During this study, four main characteristics were screened and simulated: binding affinity, molecular interactions, stability, and pharmacokinetics. Binding affinity was tested to determine how well the drug binds to the protein. In this study, RASE0125 and CARS0358 were shown to interact with Gln559, an amino acid prevalent in the G glycoprotein (Randhawa et al., 2022). Molecular interactions are studied to observe if the molecule can bind in the biologically correct way, meaning it will bind and make an effective difference. Stability is simulated to determine if the candidate will leave the site or suddenly become unstable upon binding. Finally, pharmacokinetics are simulated and screened to make sure that the molecule will actually work inside the body without any unwanted side effects. However, an artificial prediction does not

guarantee that a theorized antiviral will work in practice. Candidates still need to undergo heavy research, study, and testing (both animal and clinical) before the antiviral becomes clinically approved. While AI and machine learning are not treatments themselves, they are effective tools in determining what can be a treatment (Randhawa et al., 2022).

Nanotechnology

The primary threat of NiV lies in the highly efficient viral binding and membrane fusion mechanisms driven by the G and F glycoproteins. These mechanisms are incredibly efficient in viral infection, and currently administering and finding drugs that work against these specific mechanisms is extremely challenging. However, recent studies have been aiming to target these G and F proteins by interfering with viral entry, utilizing the properties and qualities of nanoparticles. Nanoparticles have been researched to inhibit initial viral attachment, membrane fusion, and the interaction between infected and healthy cells (Figure 4). The interaction between infected and healthy cells is particularly important because of how they interact. Infected cells can come in contact with healthy cells and lead to syncytia, the merging of two cells (Kerry et al., 2019). The F and G proteins can cause the lipid bilayers of two cells to merge, allowing viral genetic material to spread from cell to cell without ever exiting the original infected cell. This presents a challenge because antivirals cannot access inside infected cells, so once a cell is infected it is hard to stop further infection. Research has shown nanoparticles can theoretically be used to prevent the initial binding of Nipah virus and selectively deliver other potential antiviral drugs (Kerry et al., 2019).

NiV presently has no clinical treatments because conventional antiviral approaches lack certain capabilities, such as target specificity, the chance for toxicity to the host, and problems with delivery in various parts of the body. One specific potential use of nanoparticles is drug delivery (Kerry et al., 2019). Nanoparticles can be designed to recognize specific chemical characteristics of a desired target. Additionally, nanoparticles can be engineered to allow for control over the release of drugs, which can help manage effectiveness and toxicity (Kerry et al., 2019). One major feature of various nanoparticles that can be utilized is their encapsulation ability, specifically utilizing lipid-based carriers such as liposomes and micelles. Through a hydrophobic and/or hydrophilic layer, the drugs inside the nanoparticles remain unaffected by the bloodstream, allowing a safe transport from administration site to the infected site. One final reason why nanoparticles have a promising future in the fight against NiV is their permeability. The blood-brain barrier (BBB) protects the brain through a very selectively permeable surface, preventing many foreign substances - such as antivirals - from entering (Kerry et al., 2019). Since nanoparticles can be engineered to extremely microscopic sizes, they can pass through the BBB, which allows effective transmission to the brain to prevent encephalitis and neural damage from Nipah. Since most therapies face delivery challenges, nanoparticles can offer mechanisms to improve delivery across the BBB, therefore providing an improvement on the delivery of therapeutics to relevant tissues. However, nanoparticles are still highly experimental, since the safety of this technology is still relatively unknown, and most nanoparticle trials remain preclinical. Side effects such as long term toxicity are being studied before the field can advance further (Kerry et al., 2019).

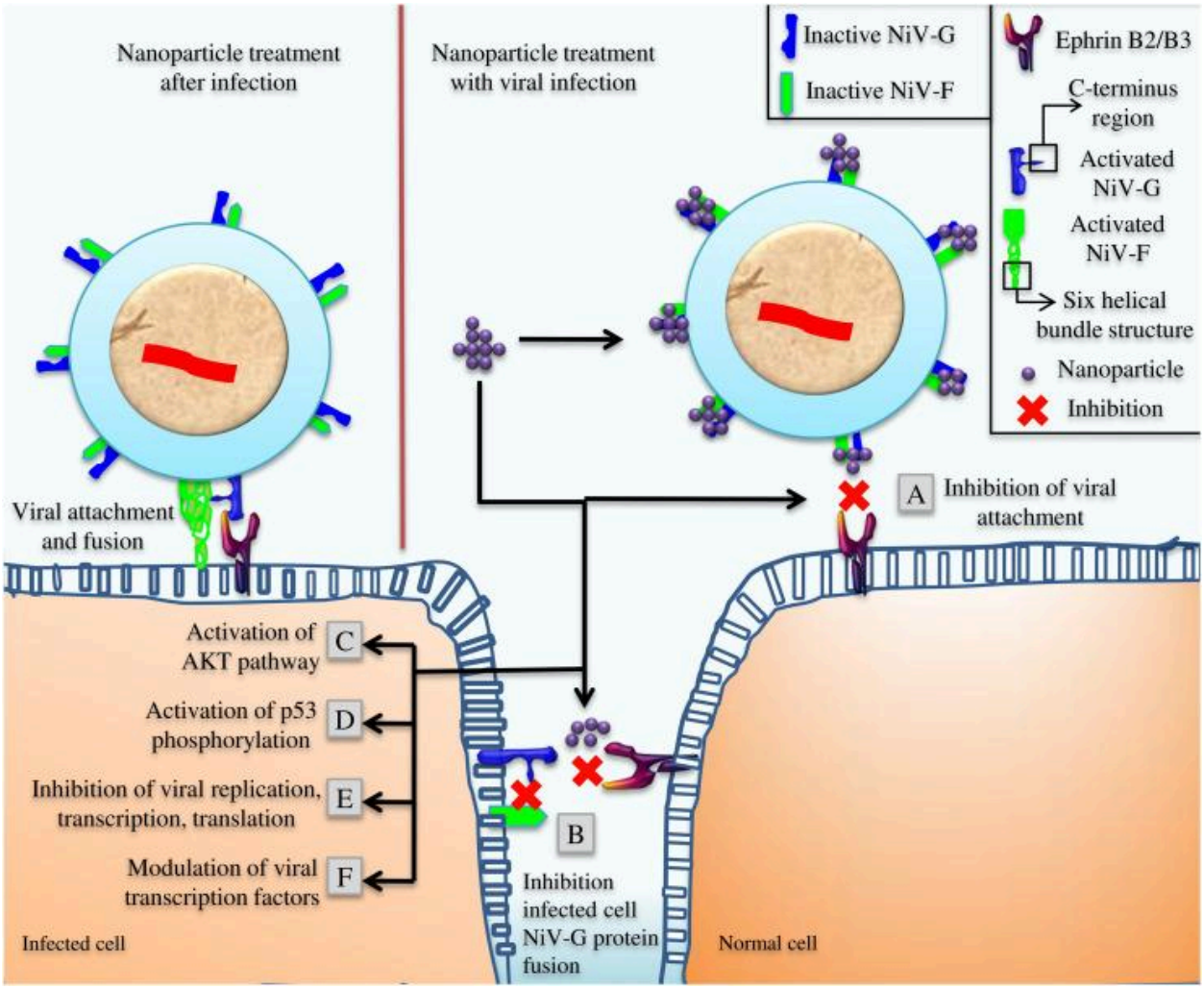


Figure 4. Various uses of nanoparticles. Reproduced from Kerry et al., 2019 with permission from the Elsevier COVID-19 Resource Centre.

Immunotherapy

While antiviral drugs and nanoparticles aim to slow or inhibit viral replication and infection, immunotherapy is designed to strengthen the immune system and immune response that fights the viral infection. Immunotherapy has recently gained attention as well, as it can target the viral proteins directly by providing antibodies that will prevent viral infection from occurring. Antibodies are immune proteins that will specifically recognize a certain molecular structure and interact with it. A monoclonal antibody is an antibody made in a lab, designed for one specific target. This is useful for immunotherapy against Nipah because scientists can engineer monoclonal antibodies to identify, recognize, and target a specific viral protein. The main proteins targeted by these administered antibodies are the G and F protein, as they are vital to binding and fusion, respectively.

Studies have recently been done regarding pre-exposure prophylaxis vaccines, meaning vaccines administered before exposure to the disease. One particular study involved research on mRNA-1215 as a pre-exposure vaccine (Ploquin et al., 2026). mRNA-1215 targets the F and

G glycoproteins of any NiV virions the immune system would encounter following administration. Scientists designed mRNA-1215 as a chimeric mRNA vaccine, meaning that scientists combined the prefusion F protein with the G glycoprotein of NiV into one antigen (Ploquin et al., 2026). This means that the vaccine aims to deliver the proper genetic material needed to prepare the immune system with defenses against any future Nipah virus infections. The study involved 40 healthy adults receiving two doses of various levels, each 4 weeks apart. The administration of the vaccine was well tolerated, with mild side effects such as myalgia and muscle aches. Few larger side effects were reported, with one case of urticaria and two cases of injection site redness and elevated temperature (Ploquin et al., 2026). Participants successfully developed the proper neutralizing antibodies against the vaccine's target proteins. Neutralizing antibodies are a specific type of antibody that prevent infection by directly binding to the viral surface glycoproteins of NiV, fully preventing infection. In addition to antibodies, T-cells were also produced in high concentration over time, highlighting the success of the vaccine in preparing the immune system. Additionally, the immune responses of the patients remained elevated for at least one year following treatment (Ploquin et al., 2026). However, as this was a Phase 1 trial, the vaccine is still relatively new and is currently undergoing further research before clinical approval can be secured.

In addition to studies on pre-exposure prophylaxis vaccines, the monoclonal antibody m102.4 has been researched, as it is a human neutralizing antibody. This means the antibody was made entirely from human genetic sequences, and it works to neutralize a specific virus. Additionally, m102.4 is used as a post-exposure prophylaxis, meaning the antibody is given after exposure but before the disease develops (Madhukalya et al., 2025). The monoclonal antibody m102.4 targets the G glycoprotein by interfering with the binding interaction between ephrin B2/B3 and the G glycoprotein, binding to the glycoprotein and preventing it from binding to ephrin B2/B3 (Madhukalya et al., 2025). Another antibody developed has been h5B3.1, which targets the F glycoprotein. The antibody works by binding to the F glycoprotein, ensuring it cannot engage in membrane fusion between the cell and virion, thus preventing viral entry as well (Madhukalya et al., 2025). Although promising, these antibodies and immunotherapy as a whole have not been clinically approved yet due to certain limitations. The Nipah virus can adjust and adapt to these antibodies, allowing the virus to develop escape mutations and conferring resistance over time through its high mutation rate. Additionally, more studies are required as researchers are still discovering in-vivo effectiveness and necessary statistics like quantity needed, lifespan, and safety level. Continued research to understand Nipah virus at the molecular level can allow us to further develop highly targeted therapeutic strategies such as the ones mentioned above (Madhukalya et al., 2025).

Biosecurity

As Nipah virus continues to cause concern worldwide, it is important to acknowledge the biosecurity measures that must be taken to help study, prevent, and treat NiV. Biosecurity is defined by the WHO as "a strategic and integrated concept that encompasses the policy and regulatory frameworks (including instruments and activities) that analyse and manage risk in food safety, public health, animal life and health, and plant life and health, including associate environmental risk" (Renault et al., 2022). In relation to Nipah virus, biosecurity involves strategizing and coordinating the research, prevention, and treatment of the pathogen (Renault et al., 2022). Therefore, the fundamental goals of biosecurity sectors are risk management and

disease prevention. If proper biosecurity measures are not taken, pathogens can pose serious global threats, sometimes becoming epidemics, such as SARS-CoV-2. As pathogens like Nipah virus begin to become more prominent, it is important the proper methods are taken in order to prevent future large-scale outbreaks.

Nipah virus presents an especially challenging threat to handle, as several factors must be considered. NiV is a zoonotic disease, perfectly falling into the biosecurity realm. As zoonotic diseases are spread from animal to human, both animal health and human health must be considered when researching possible prevention methods. Failure to protect both human health and animal health can still result in outbreaks, as NiV will continue the viral replication process in either host. As such, the population of reservoir hosts, vectors, and humans, must be studied, as well as their interactions. As previously mentioned, Nipah virus cannot be contained merely by treating patients as cases arrive, research must be done to prevent the movement between various populations. Animal health may be monitored by preventing further infection in susceptible populations. Human health may be monitored by controlling outbreaks and infection, as well as limiting transmission via quarantining. Additionally, environmental factors play a massive role in the management of the virus, observing the ecological conditions that can allow interactions that will cause infection. Essentially, biosecurity specialists must identify potential hazards, assess how these hazards could spread, and implement measures to reduce these risks. However, the risk of complications in these plans is high. The high mortality, respiratory complications, and neurological complications of NiV make it hard to treat cases as they arrive. Additionally, the difficulty to deliver early diagnoses poses a challenge, especially because early onset symptoms resemble several other illnesses. Providing care and treatment for such a rapidly growing problem has proven to be difficult due to the human-to-human transmission rates, as well as the BSL-4 classification of Nipah virus (Madhukalya et al., 2025). BSL-4 pathogens require a designated, highly secured laboratory, with special protective equipment being required at all times during active study. As Nipah virus poses a very large threat to global health, scientists, researchers, and government organizations have been working hard to find a method to combat this pathogen.

In order to research the prevention and treatment of NiV, several participants in the biosecurity industry must collaborate and pool resources (Figure 5). As highlighted in the concept of “One biosecurity", strengthened collaboration between several sectors in the biosecurity field must take place. Governments, private investors, and private research institutes must all work together and share resources (Renault et al., 2022). Together, several sectors can work together to create a highly necessary protective plan, consisting of several layers of research and risk management. As no clinically approved vaccines currently exist, constructing such a plan poses several challenges. However, as research continues, new technologies can serve as potential utilities in NiV prevention plans. Scientists can utilize AI models to quickly develop drugs and chemicals that can effectively inhibit or combat the virus, and nanotechnology can be used to administer, detect, and even inhibit NiV itself. Liposomes and micelles have shown to be effective administration technologies, and the various compositions of nano molecules can deliver several different abilities to aid medical professionals. When paired with the possibilities presented by strengthening the body via immunotherapy, several possibilities for treating Nipah virus emerge. Although these technologies are still fairly new and not thoroughly tested, they show promise for future integration into NiV treatment and prevention plans. The future of NiV and the world is unclear, but if the proper biosecurity

measures are taken and every sector of the field can combine efforts, it is possible that a plan to treat, combat, and prevent this disease will emerge.

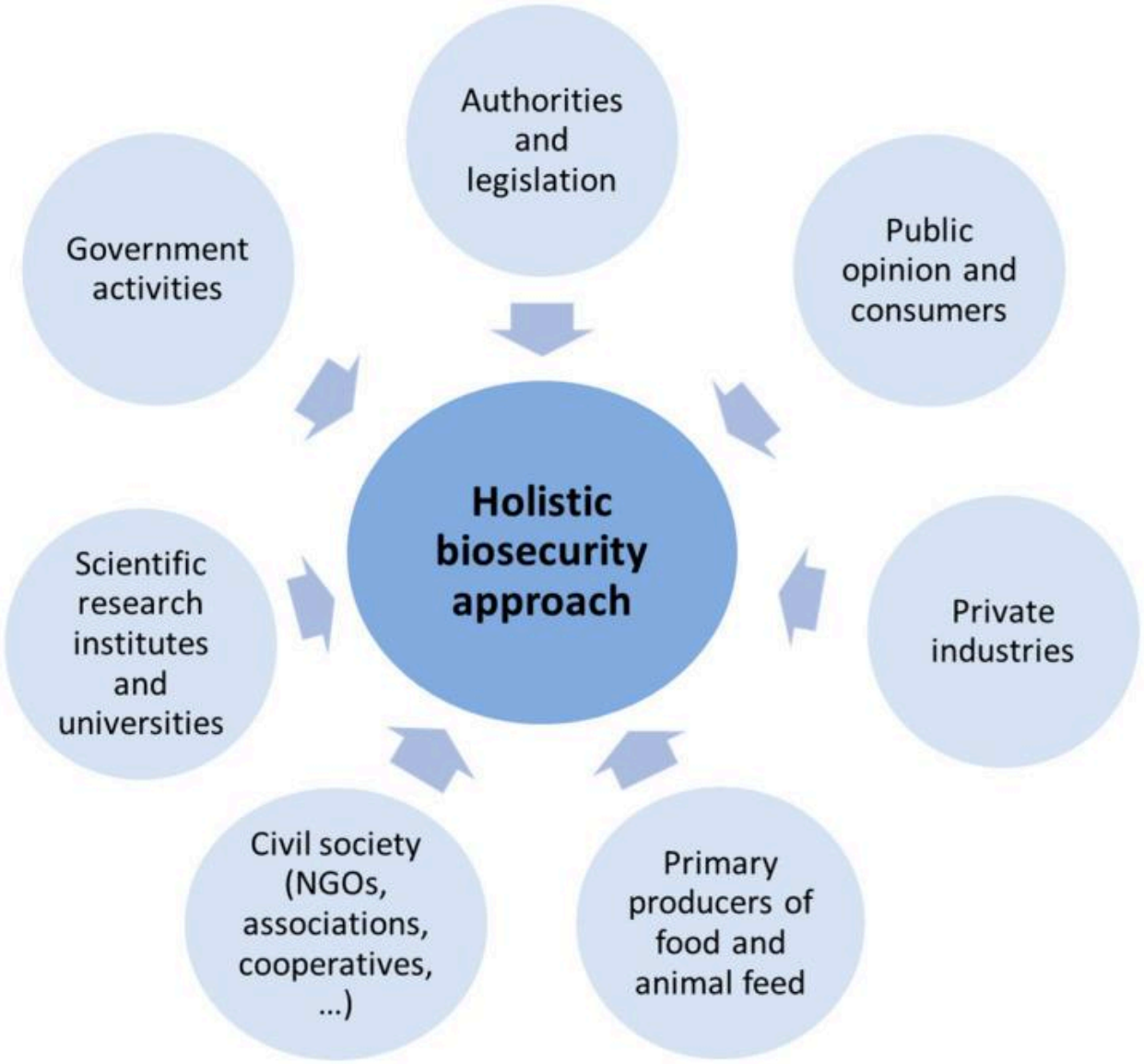


Figure 5. Different sectors of the biosecurity approach. Reproduced from Renault et al., 2022 [5] under the terms of the Creative Commons Attribution 4.0 International License.

Conclusion

Nipah virus has recently gained attention due to its classification as a highly pathogenic zoonotic virus, as it spreads from animals to humans at an alarming rate, causing outbreaks very frequently. The natural reservoir of the virus is the *Pteropus* fruit bat, of which 2 species are the main reservoir hosts. Molecularly, NiV possesses a non-segmented, negative-sense RNA genome, meaning it requires a RNA dependent RNA polymerase to replicate itself. It engages in infection through 2 of its glycoproteins, F and G. Upon infection, the replication and spread of the disease will lead to respiratory and neurological disease. The mechanism NiV uses to enter

and infect host cells contributes to its rapid ability to spread and cause infection, and the persistent presence of the virus in the natural reservoir creates several, frequent opportunities for spillover.

Currently, Nipah virus has no clinically approved treatments, and all treatments are mainly supportive. However, recent researchers have begun pushing new fields in attempts to find creative solutions to combat this virus. AI and machine learning models have been used to narrow down and identify possible compounds, test their docking ability, and observe molecular interaction and stability all through simulations. This has allowed researchers to save time on identifying candidates for antiviral drugs, while creating efficient ways to observe steps of the research process without having to physically create the molecule. Another method being developed is nanotechnology, which can serve as an antiviral administration tool or an inhibitor itself. The size of the nanoparticles allows an effective, fast, and efficient transmission and delivery of antiviral drugs, improving the stability, targeting, and release of antivirals. Finally, immunotherapy has also been researched to handle Nipah virus. Immunotherapy with regard to Nipah deals with developing antibodies that the human body can use to directly combat the virus and viral infection, with current research aiming to target the G and F glycoproteins. Monoclonal antibodies m102.4 and h5B3.1 target the attachment of the G glycoprotein and the fusion of the F glycoprotein, respectively. Overall, AI has assisted in the discovery and early stages of drug testing, nanotechnology has shown promise in the efficient delivery and administration of drugs, and immunotherapy has helped scientists understand how to specifically target and neutralize Nipah virus at the molecular level.

The rapid increase in concern regarding Nipah virus has led to an increase in the relevance of biosecurity. Biosecurity is classified as the strategies and methods implemented to treat and prevent any health risks, whether it be from food or from a pathogen as dangerous as NiV. Biosecurity fields aim to contain, combat, and manage the spread of Nipah virus in order to prevent any dangerous outbreaks. However, this is highly challenging, as the severe side effects and human-to-human transmission of NiV makes it hard to safely contain and research. In order to prevent further outbreaks, human health, animal health, and ecological factors must be taken into account. However, if all sectors of biotechnology collaborate in order to fight this pathogenic threat, then it is possible to develop a structured, multi-layered prevention and treatment plan. Researchers can potentially use AI, nanotechnology, and immunotherapy in said plans, but until these three methods receive clinical approval, no further action can be made with them. Although the threats posed by Nipah virus are large, the future is promising.

The Nipah virus is undoubtedly a large threat to global health. The severe symptoms, high mortality rate, and rapid transmission are all causes for concern amongst medical health professionals worldwide. However, it is possible to combat this pathogen with the help of new technology and a collaborative industry. Although the virus has high mutation rates and is extremely adaptable, researchers, scientists, governments, and medical health professionals are working together to develop a way to prevent this illness from escalating. With the continued research and development of new technologies, Nipah virus can be treated, contained, and prevented from causing any further risk.

Acknowledgement

This paper was written in collaboration with the Polygence Research Program, under the mentorship of Yarden Edomi.

References

Kerry, R. G., Malik, S., Redda, Y. T., Sahoo, S., Patra, J. K., & Majhi, S. (2019). Nano-based approach to combat emerging viral (NIPAH virus) infection. *Nanomedicine: Nanotechnology, Biology and Medicine, 18*, 196–220. https://doi.org/10.1016/j.nano.2019.03.004

Lin, H., Vogel, H., & Zhang, H. (2026). A comparative review of artificial intelligence applications in small molecule versus peptide drug discovery. *International Journal of Molecular Sciences, 27*(7), 3142. https://doi.org/10.3390/ijms27073142

Madhukalya, R., Yadav, U., Parray, H. A., Raj, N., Lakshmanan, S. S., Agarwal, V., Anand, A., Kumar, D., Das, S., & Kumar, R. (2025). Nipah virus: Pathogenesis, genome, diagnosis, and treatment. *Applied Microbiology and Biotechnology, 109*(1), 158. https://doi.org/10.1007/s00253-025-13474-6

Ploquin, A., Mason, R. D., Holman, L. A., Happe, M., Widge, A. T., Novik, L., Ortega-Villa, A. M., Yamshchikov, G. V., Gordon, I. J., Ola, A., Arthur, A., Costner, P. J. M., Mendoza, F., Saunders, J., Wang, X., Whalen, W. R., Utoh, J., Cunningham, J., Loftus, L. N., ... Dropulic, L. K. (2026). A structure-based mRNA vaccine for Nipah virus in healthy adults: A phase 1 trial. *Nature Medicine, 32*, 1401–1410. https://doi.org/10.1038/s41591-026-04265-1

Randhawa, V., Pathania, S., & Kumar, M. (2022). Computational identification of potential multitarget inhibitors of Nipah virus by molecular docking and molecular dynamics. *Microorganisms, 10*(6), 1181. https://doi.org/10.3390/microorganisms10061181

Renault, V., Humblet, M.-F., & Saegerman, C. (2022). Biosecurity concept: Origins, evolution and perspectives. *Animals, 12*(1), 63. https://doi.org/10.3390/ani12010063

Pellett, P. E., Mitra, S., & Holland, T. C. (2014). Basics of virology. *Handbook of Clinical Neurology, 123*, 45–66. https://doi.org/10.1016/B978-0-444-53488-0.00002-X