

## Development of airways protection against respiratory Nipah virus infection by inhalation of antiviral peptides

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**Introduction:** Nipah virus (NiV) is a recently emerged zoonotic paramyxovirus, capable of inter-human transmission and listed by WHO among the top eight emerging pathogens, based on the probability of causing severe outbreaks and a pandemic potential. In humans, NiV induces acute respiratory distress and encephalitis with a lethality of 40-100%. A novel antiviral approach, based on peptides which interfere with the fusion of NiV with host cells has been recently developed.

**Research hypothesis:** The project aims to develop a new approach to administer aerosolized peptides capable of inhibiting respiratory NiV infection, which may be applied to the other respiratory viruses using similar fusion mechanism for viral entry.

**Methods:** We have developed an inhalation strategy using nebulized antiviral peptide in African Green Monkey (AGM), an animal model shown to well reproduce human NiV infection.

**Results and discussion:** A customized nebuliser with a specific mesh size and interface to produce an aerosol of peptides while ensuring the upkeep of >90% of antiviral activity after nebulisation was assessed. Lung deposition was measured by *in vivo* scintigraphy (8-16% in terms of nebulizer charge). Toxicology analysis in AGM demonstrated the absence of adverse lung findings from nebulised peptides after several consecutive administrations of 10 min. Immunofluorescence assays, using peptide specific antibodies on lung slices, revealed the presence of peptides along the respiratory tract 24 h after administration.

**Conclusion:** Developed nebulisers are now ready for the first proof-of-concept study with the infectious NiV in a Biosafety level 4 laboratory. The results may open new perspectives for antiviral prevention against respiratory viruses and the strategy could be further extended to the ongoing SARS-CoV-2 outbreak (funded by DGA-ANR-Astrid-Maturation).