

# IMPERIAL

## Effects of an anti-viral interferon booster, RIG-I agonist (RIG-101), on influenza infection *in vitro* and *in vivo*

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# Conflict of interest disclosure

I have no real or perceived conflicts of interest that relate to this presentation.

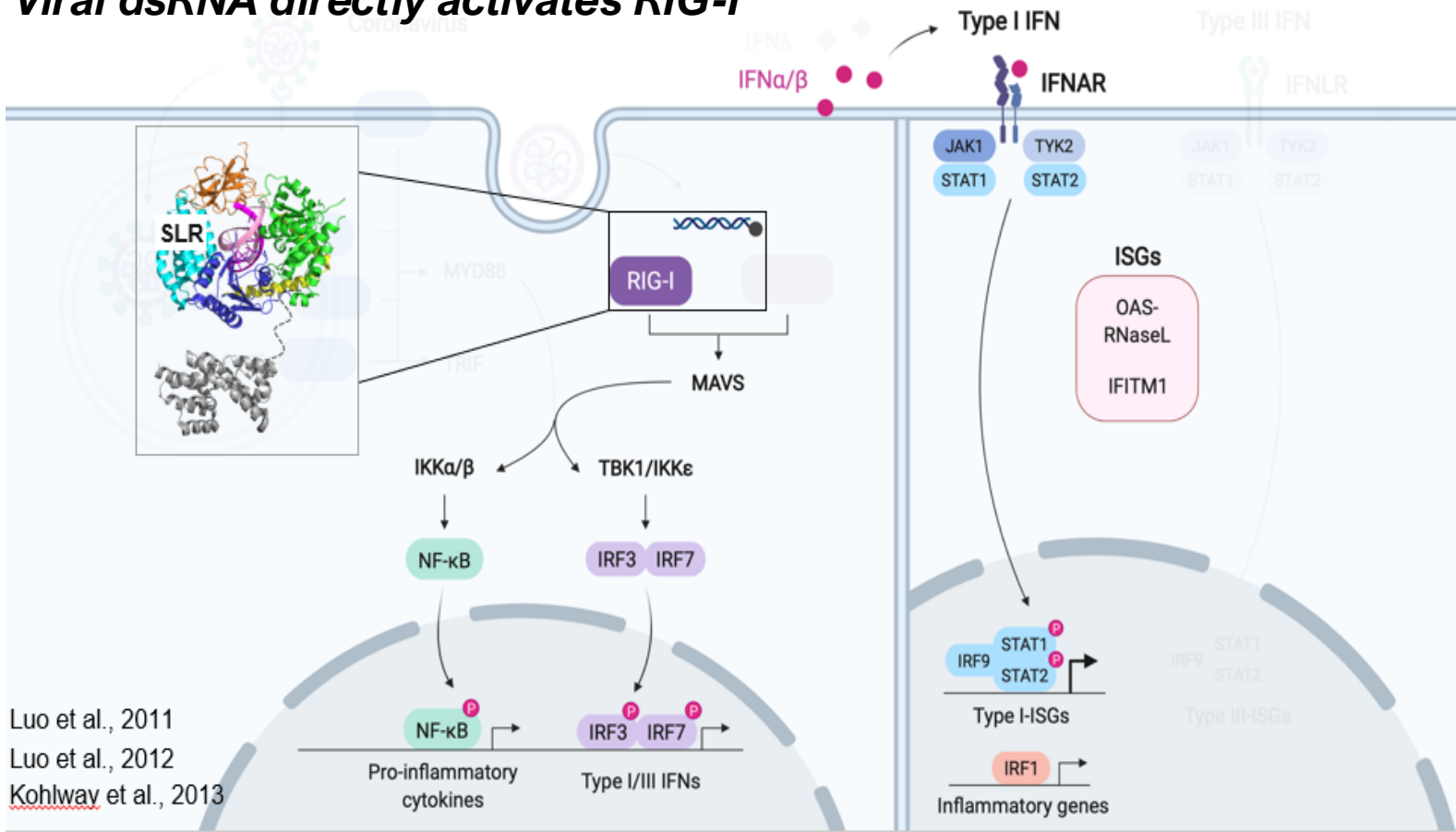
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Grants/research support:	RIGImmune Inc.
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# RIG-I – first line of defence against RNA viral pathogens

## *Viral dsRNA directly activates RIG-I*



- Antiviral response by ISGs (interferon stimulating gene) through IFN pathway.

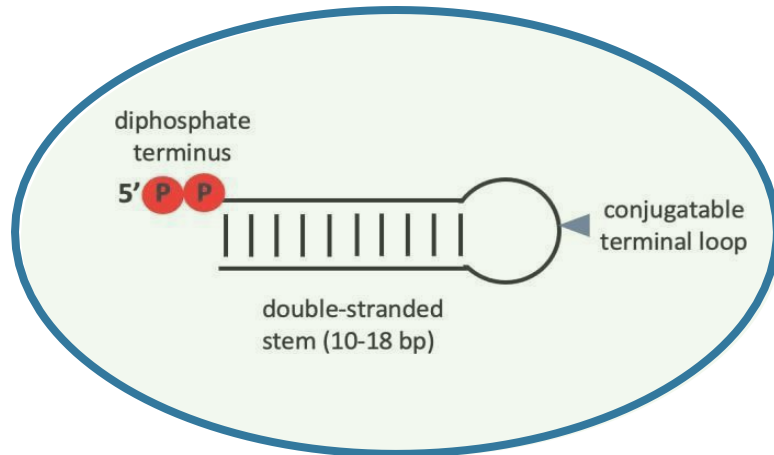
Luo et al., 2011  
Luo et al., 2012  
Kohlway et al., 2013

# RIG-101 a synthetic RIG-I agonist delivered in novel NEED™ formulation

## RIG-101

(Synthetic stem loop RNA)

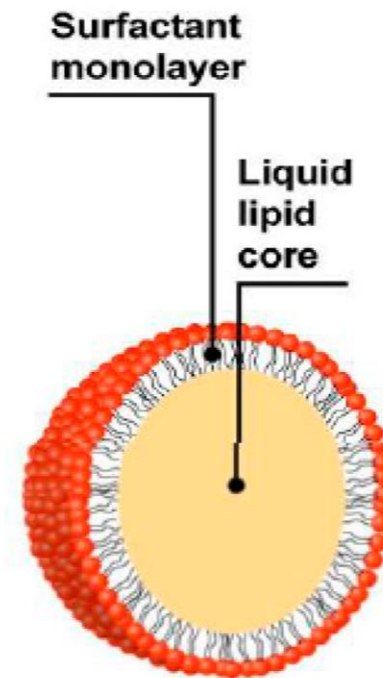
- RIG-101 is optimized to be a highly selective RIG-I agonist.



## NEED™

(Nano-Emulsion Enhanced Delivery)

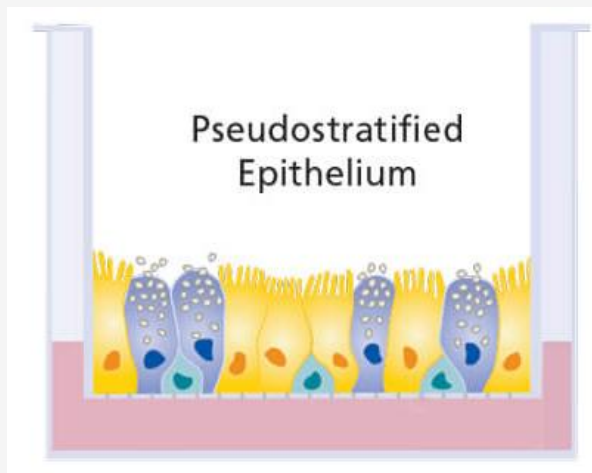
- Novel non-LNP delivery system
- Proprietary transformation of surfactants and fatty acids into a nano-emulsion complex (non-LNP) that encapsulates a nucleic acid payload with control of particle size and charge (RIGImmune Inc. patent pending).



# A single dose of RIG-101 NEED™ induces potent and long-lasting interferon signalling with only transient proinflammatory signal (innate immunity) in air-liquid interface (ALI) human nasal epithelium

## Apical Treatment

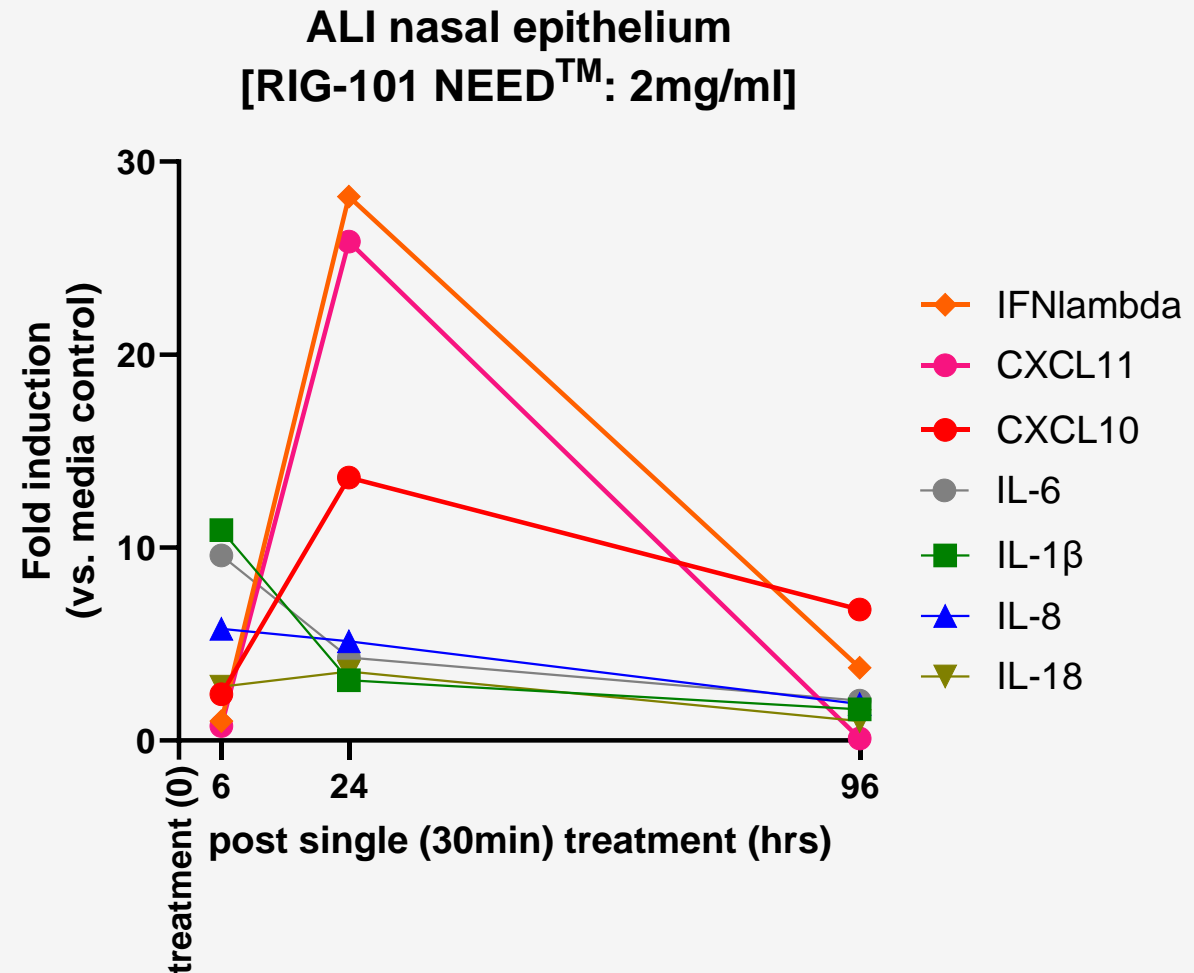
50µL, 30min



Air liquid interface (ALI)  
Cultured human nasal  
epithelium  
[MucilAir™ nasal pool]

6, 24, 96hrs

Apical  
wash  
collection

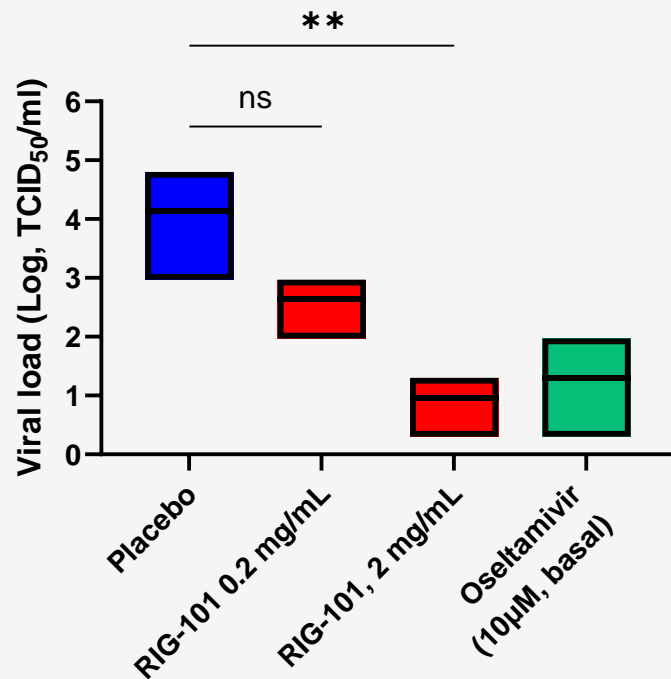


Cytokines were measured using MSD platform.

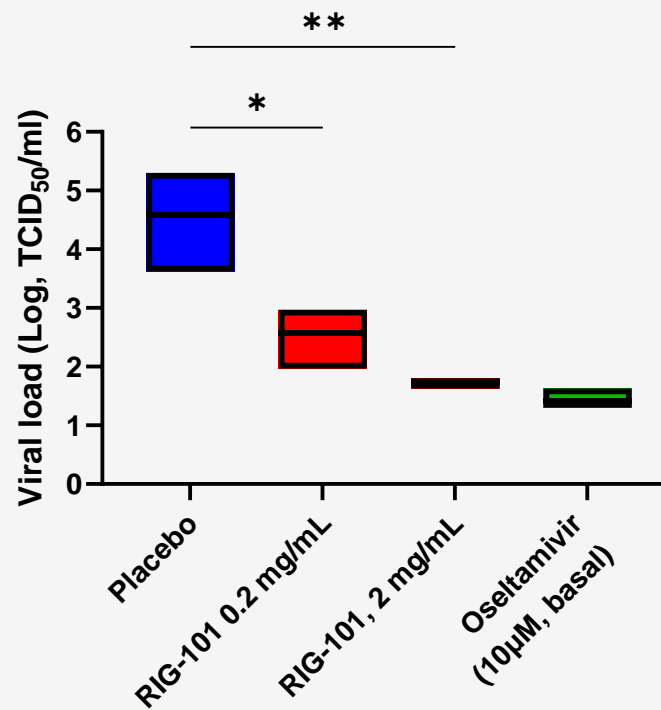
# Prophylactic treatment of RIG-101 NEED™ reduces influenza viral load in ALI nasal epithelium-a highly translatable model



Viral load (DAY2)  
[RIG-101 NEED™]

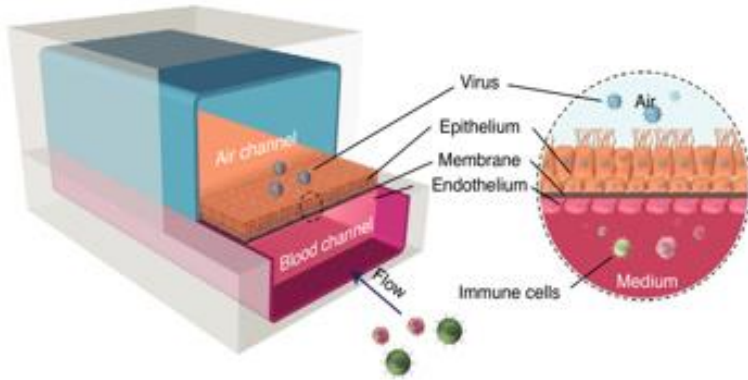


Viral load (DAY3)  
[RIG-101 NEED™]



RIG-101  
2 mg/mL = approx. 200µM  
0.2 mg/mL = approx. 20µM

# Prophylactic treatment of RIG-101 NEED™ reduces influenza viral load in Bronchial (HBEC3-KT)-on-a-chip



Day -1: Treatment at apical surface (30 min +)

Day 0: Collect apical wash for CXCL10 measurement

Day 0: H1N1PR8 ( $4 \times 10^5$  PFU/ml, 500 $\mu$ L at 1000 $\mu$ L/hr for 3-4min) infection  
(incubation for 1hr)

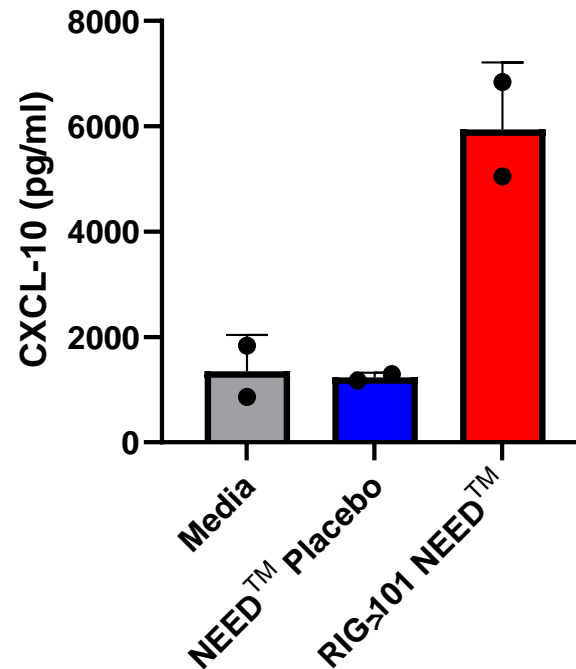
Day 1,2,3,6: Apical wash collection

HBEC3KT: immortalized human bronchial cell line capable to form pseudostratified epithelium under ALI culture

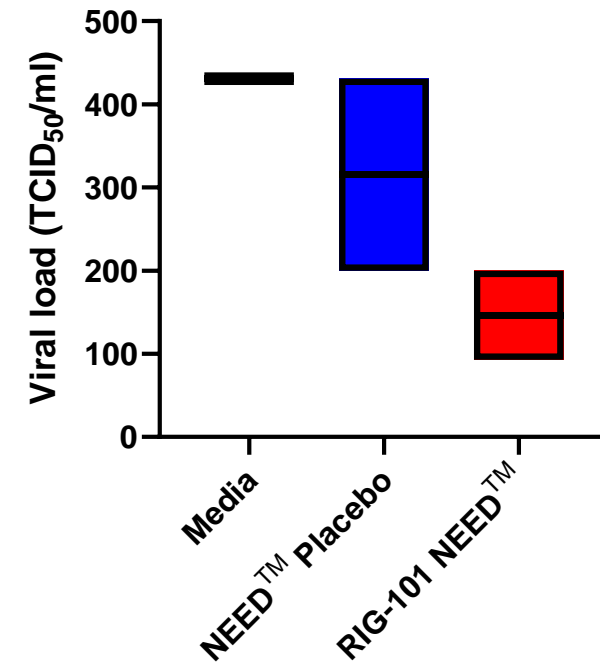
NEED™ Placebo  
RIG-101 NEED™: 2mg/ml

Apply 500 $\mu$ L at 300 $\mu$ L/hr, the 30min incubation

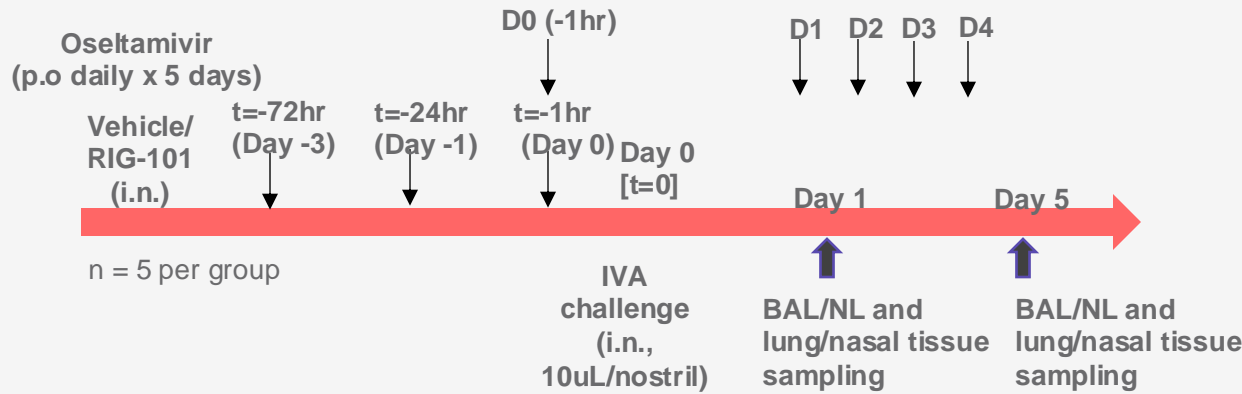
**CXCL10 release in apical wash  
[a day post RIG treatment]**



**Viral load in apical wash  
[H1N1/PR8, D3 pi]**



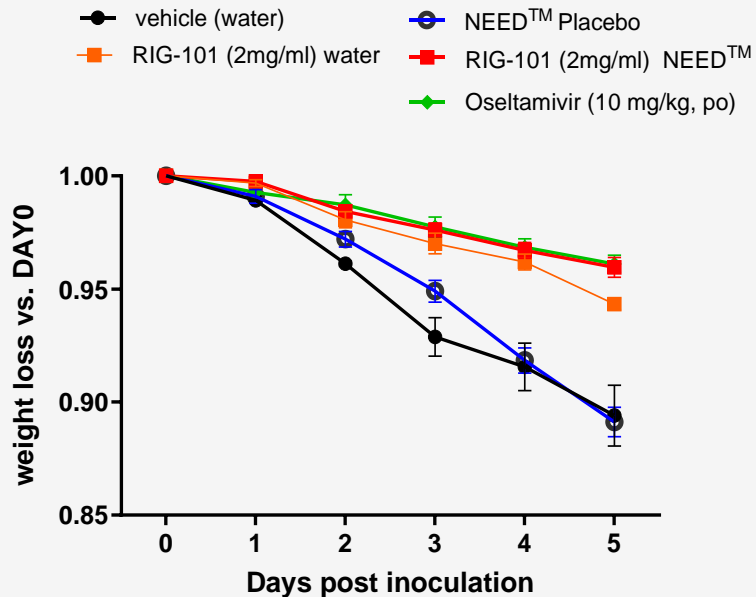
# Intranasal RIG-101 NEED™ reduces influenza (H1N1, PR8) viral load and neutrophilia in nose of influenza infected mice



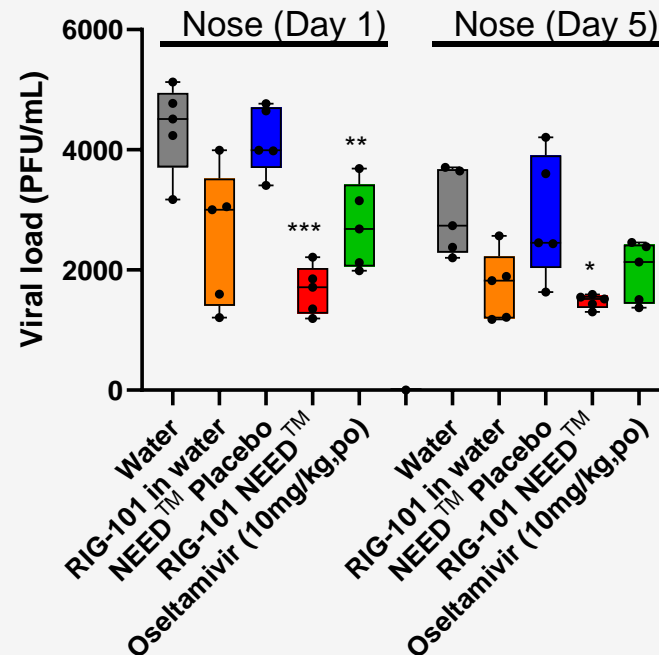
Sub-lethal influenza A H1N1 (PR8) model

RIG-101 and dosing method:  
10µL per nostril (-72 hrs, -24hrs, -1hr)

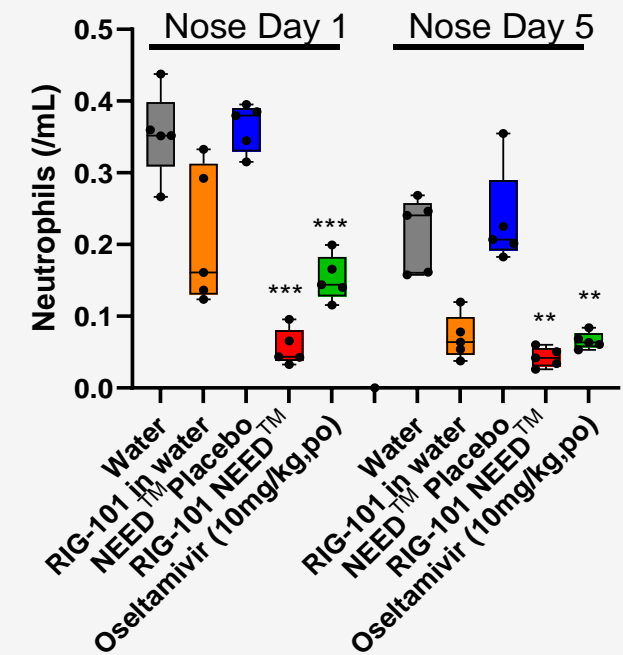
## Reduced body weight loss



## Reduced viral load in nose



## Reduced inflammation (neutrophil infiltration)





# Summary

RIG-101 was found to show significant induction of type I/III interferon signalling, and potent antiviral effects against influenza *in vitro* and *in vivo*.

# Conclusion

This suggests that topical prophylactic treatment of RIG-101 has potential to show viral prevention efficacy against influenza infection.

# IMPERIAL

Thank you!



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