Yale University School of Medicine

SMNR 21

# Low Ambient Humidity Impairs Barrier Function and Innate Resistance Against Influenza Infection

Eriko Kudo
Yale university,
school of medicine
eriko.kudo@yale.edu

ORLANDO
2020 WINTER CONFERENCE AND AHR EXPO

## *Acknowledgements*

The Howard Hughes Medical Institute

The Condair Group

The Naito Foundation

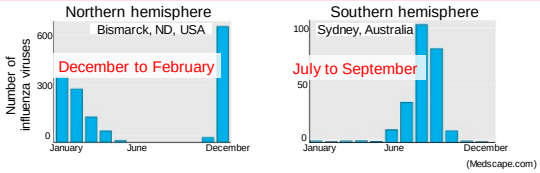
National Institutes of Health Grants

## *Learning objective*

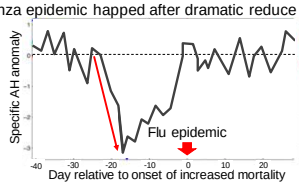
- Provide a data-driven description of indoor environmental factors that are associated with occupant health
- Explain the application of energy-saving and hygienic approaches to active humidification when supplementation is necessary as an intervention for dry air
- Provide building owners a cost-benefit analysis of occupant health as a building performance metric
- identify the relationship between water in the liquid and vapor state and the human body



## *Seasonal influenza and winter months*




Influenza epidemic happed after dramatic reduce of humidity.




**Humidity is correlated with influenza epidemic and transmission.**

(Shaman et al, Plos Biol 2010)

## *Learning objective*

- Understand the importance of humidity for protection against influenza infection
- Understand the effect of humidity for immune system

## *Influenza virus*

- Influenza is an infectious respiratory disease by influenza virus.
- Negative-sense single-strand RNA viruses with a segmented genome.
  - Influenza virus A
  - Influenza virus B
  - Influenza virus C

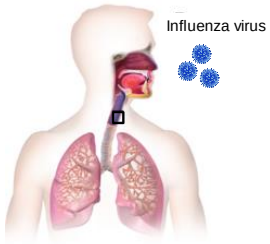
  ] Main cause of the seasonal influenza epidemic


Influenza virus

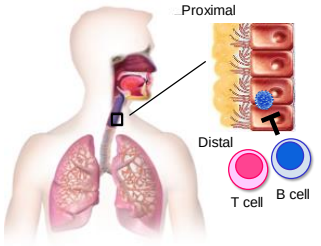
- Infects 5-10% of adults and 20-50% of children globally every year
- Annual epidemics of influenza result in ~1 billion infections, 3–5 million cases of severe illness and 300,000–500,000 deaths.
- Symptoms: fever, sore throat, runny nose, cough, headache, muscle pain, pneumonia

## *How do we remove influenza virus from our body?*

Influenza virus is spread from infected people by cough or sneeze.

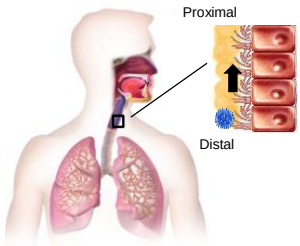



## *The host immune defense against influenza*




1. **Physical barrier**: Mucus production and ciliary clearance
2. **Innate immune responses**: Type I IFN and Interferon stimulated genes (ISGs)
3. **Adaptive immune response**: Producing antibody and cytokine from T cells and B cells

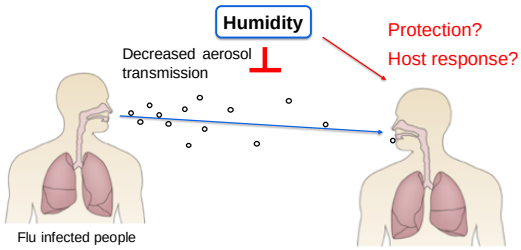
## *The host immune defense against influenza*




1. **Physical barrier**: Mucus production and ciliary clearance

**First line of defense against pathogen.**

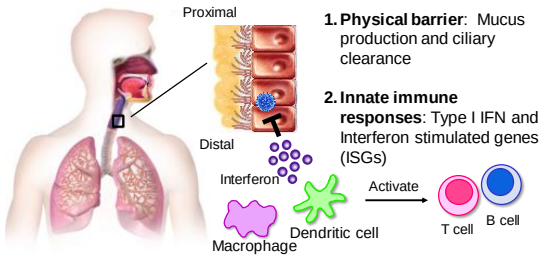
## *Purpose: The impacts of humidity on host response to flu infection and disease outcome*




**Can high humidity protect influenza virus infection and disease in mice model?**

**How does humidity protect influenza virus infection?**

## *The host immune defense against influenza*




1. **Physical barrier**: Mucus production and ciliary clearance
2. **Innate immune responses**: Type I IFN and Interferon stimulated genes (ISGs)

## *Environmental chamber model system: Humidity*

**Condition**

Mouse room: 20-22°C, 50% relative humidity (RH).

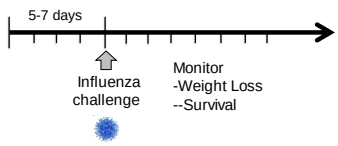
Dry Low humidity(10-20%RH)

Normal High humidity (50%RH)

All 20°C

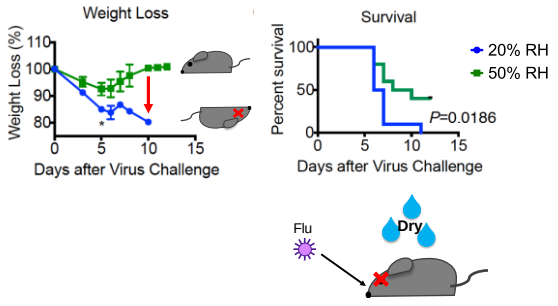
Environmental chamber

**Experimental design**



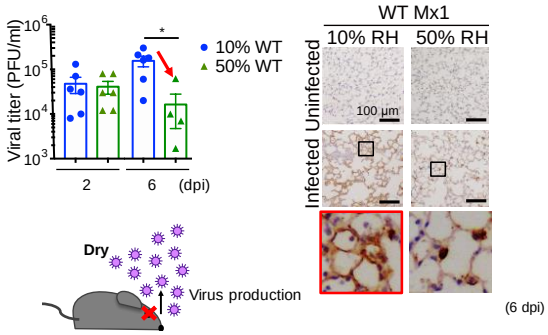

hvPR8 (IAV) influenza infection by intranasal or aerosol inoculation

## *Low humidity leads to more severe disease*



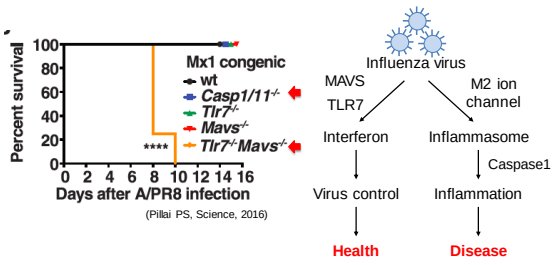

**10% humidity increased severe disease.**

## *Low humidity impairs influenza virus clearance*



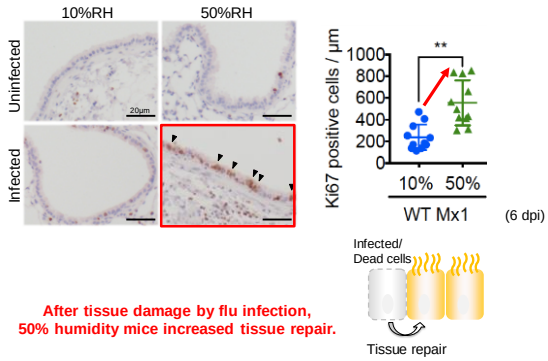

**10% humidity increased virus infection and replication.**

## *Antiviral resistance and disease tolerance in influenza*



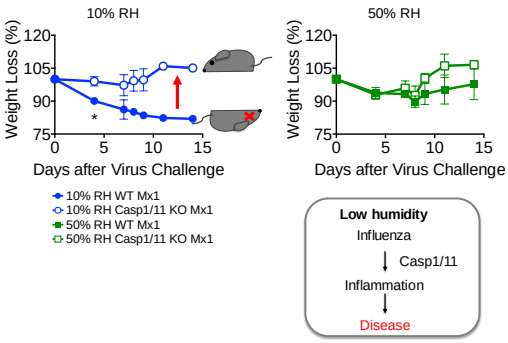

Does Caspase 1/11 signaling mediate increased disease severity at low humidity?

## *Low humidity impairs tissue repair in mice trachea*

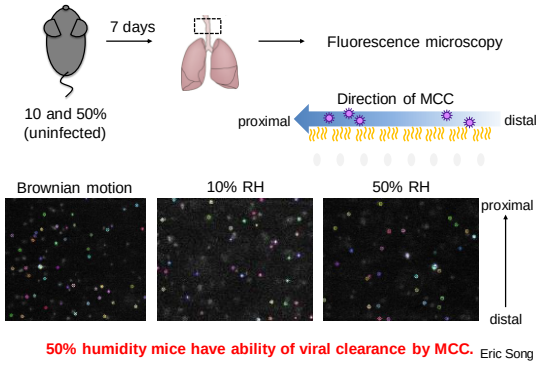



**After tissue damage by flu infection, 50% humidity mice increased tissue repair.**

## *Low humidity leads to more severe disease thorough caspase1/11*

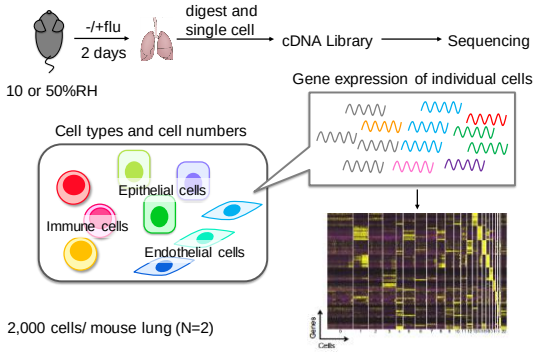



## *Low humidity decreases mucociliary clearance (MCC)*

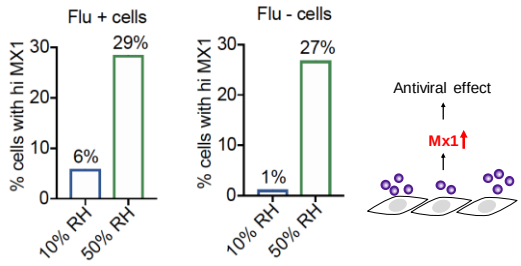



**50% humidity mice have ability of viral clearance by MCC.** Eric Song

## *Single cell RNA-sequencing provides the expression of individual cells*



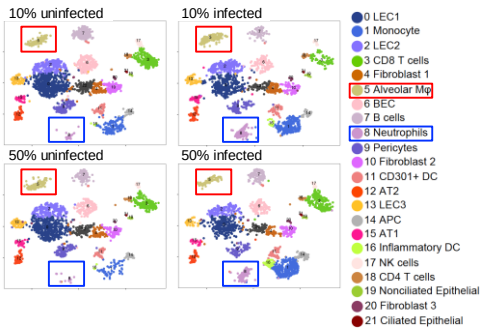

## *IFN-induced Mx1 were suppressed in both infected- and uninfected cells*




**50% humidity enhances antiviral response.**

Eric Song

## *There are 22 distinct cells cell types in whole lung*

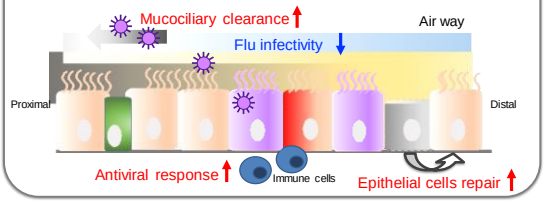



Eric Song

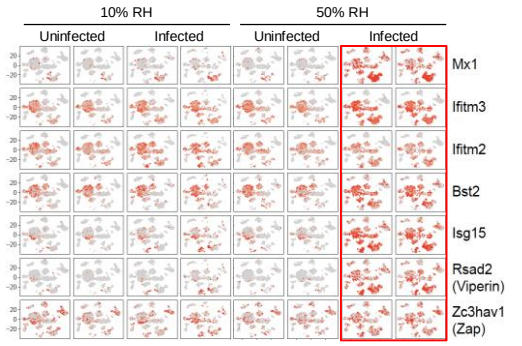
## *Summary*

1. Low humidity increased susceptibility to infection and more severe disease.
2. Low humidity decreased epithelial turnover after influenza infection.
3. Low humidity attenuated mucociliary clearance of influenza virus.
4. Low humidity suppressed antiviral response such as IFN-induced Mx1.

**Increasing ambient humidity may be a viable strategy to reduce disease symptoms and to promote more rapid recovery in influenza-infected individuals.**




## *Low humidity decreases ISGs expression*




**50% humidity highly express antiviral response genes.**

Eric Song

## *How to control humidity in our life*

Wearing face mask

(sankei.com)

Control humidity by humidifier


Humidity control is necessary in hospital, school, office and airplane.

## *Bibliography*

Kudo E, E Song, LJ Yockey, T Rakib, PW Wnag, RJ Homer and A Iwasaki

Low ambient humidity impairs barrier function and innate resistance against influenza infection. ***Proc Natl Acad Sci U S A***, 2019, 116 (22), 10905-10910

## *Questions?*

Eriko Kudo

eriko.kudo@yale.edu