Indoor Air Pollution and TB Infection:
Findings from a Prospective Cohort Study

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Research Question:
Why do only ~25% of close contacts develop TB infection?

- Known TB transmission risk factors
  - Infectiousness of Index Case (bacillary load)
    - AFB smear positive
    - Cavitary TB
  - M. tuberculous strain: e.g., Beijing strain more infective
  - Contact duration and proximity
  - Poverty: crowding and malnutrition
- Unclear environmental risk factors
  - Air pollutants: Indoor air pollution, Outdoor air pollution, Secondhand smoke?

Hypotheses

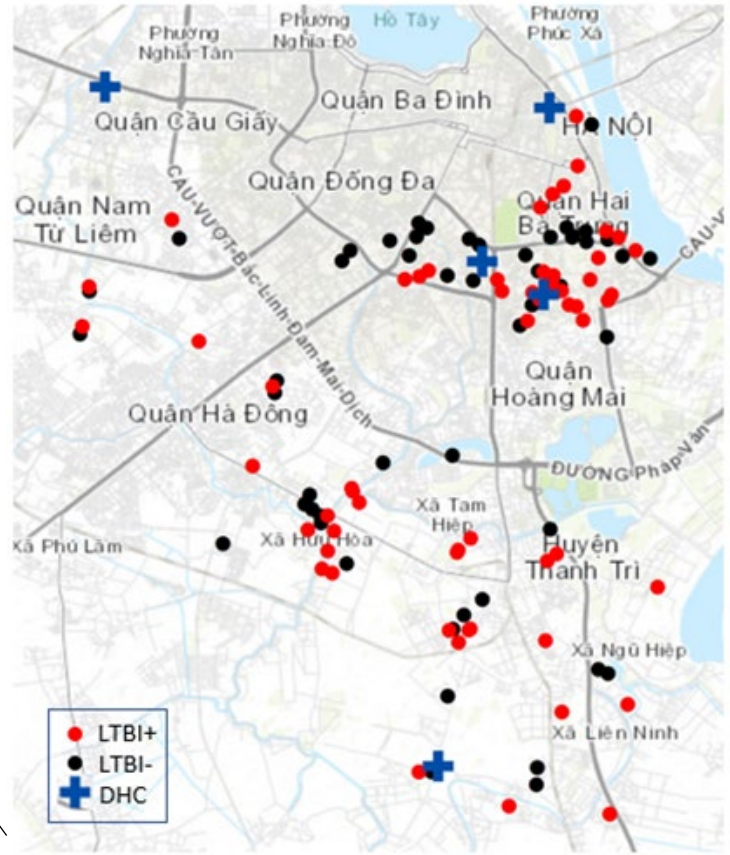
Southeast Asian urban indoor air pollutants are associated with:

1. Increase TB infection among child household contacts of active TB patients

2. Decrease innate immune responses to *Mycobacterium tuberculosis*

Prospective cohort study of household contacts in Vietnam

- 73 index cases
- 109 healthy children living with TB patient
- Follow quarterly, 1 yr
- Determine air pollutant exposures
- Tuberculin Skin Testing



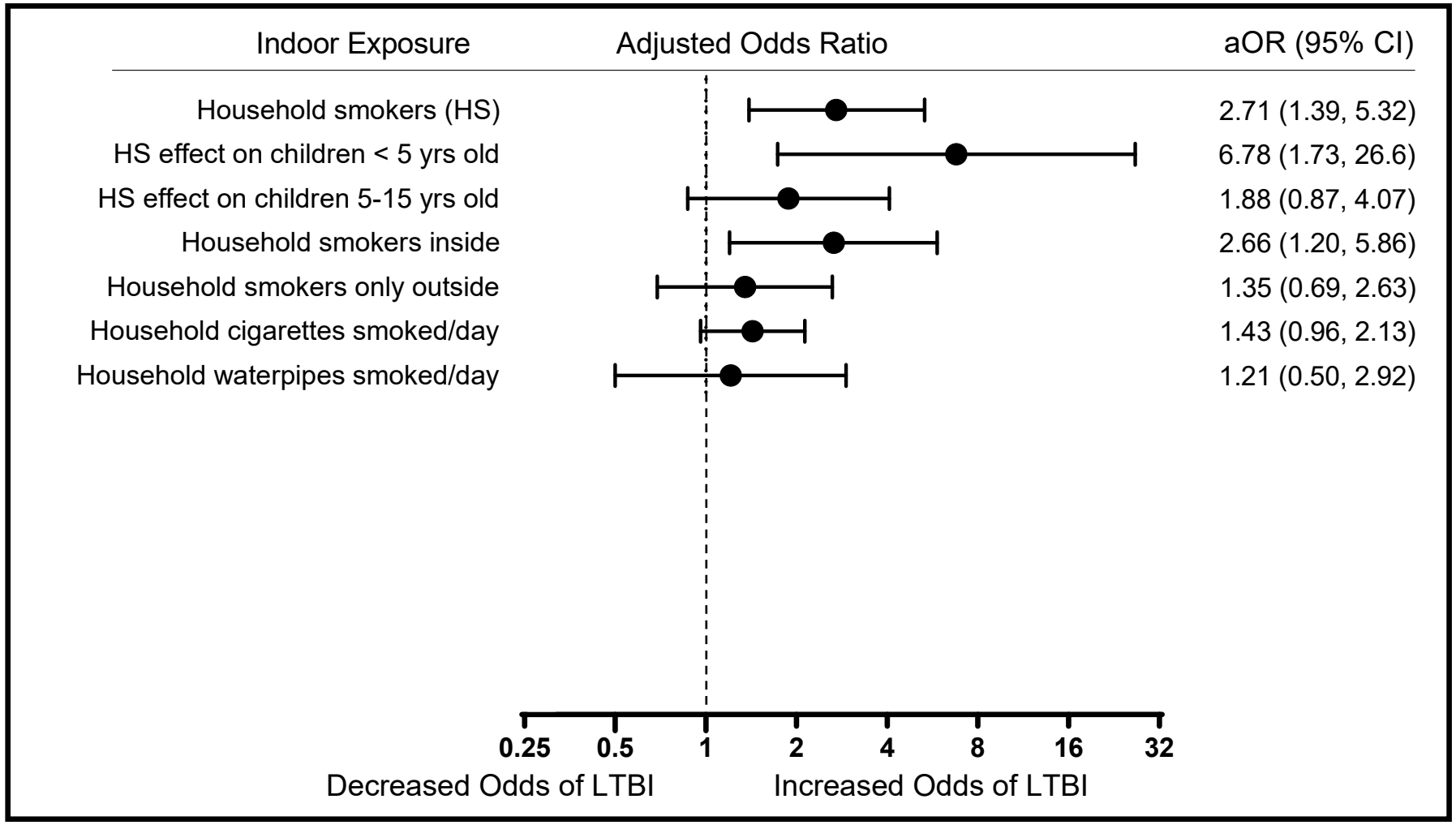
Blount & Nahid, AJRCCM 2021

Smoking in Vietnam

- 50% of men smoke
- 70% of Vietnamese report exposure to Secondhand smoke (SHS)
- Cigarettes
- Waterpipe: 13% of smokers
- Assess SHS exposure with questionnaire

Global Adult Tobacco Survey, 2015
Global School-Based Student Health Survey, 2013
Xuan, Prev Chronic Dis 2013

Secondhand smoke increases odds of infection



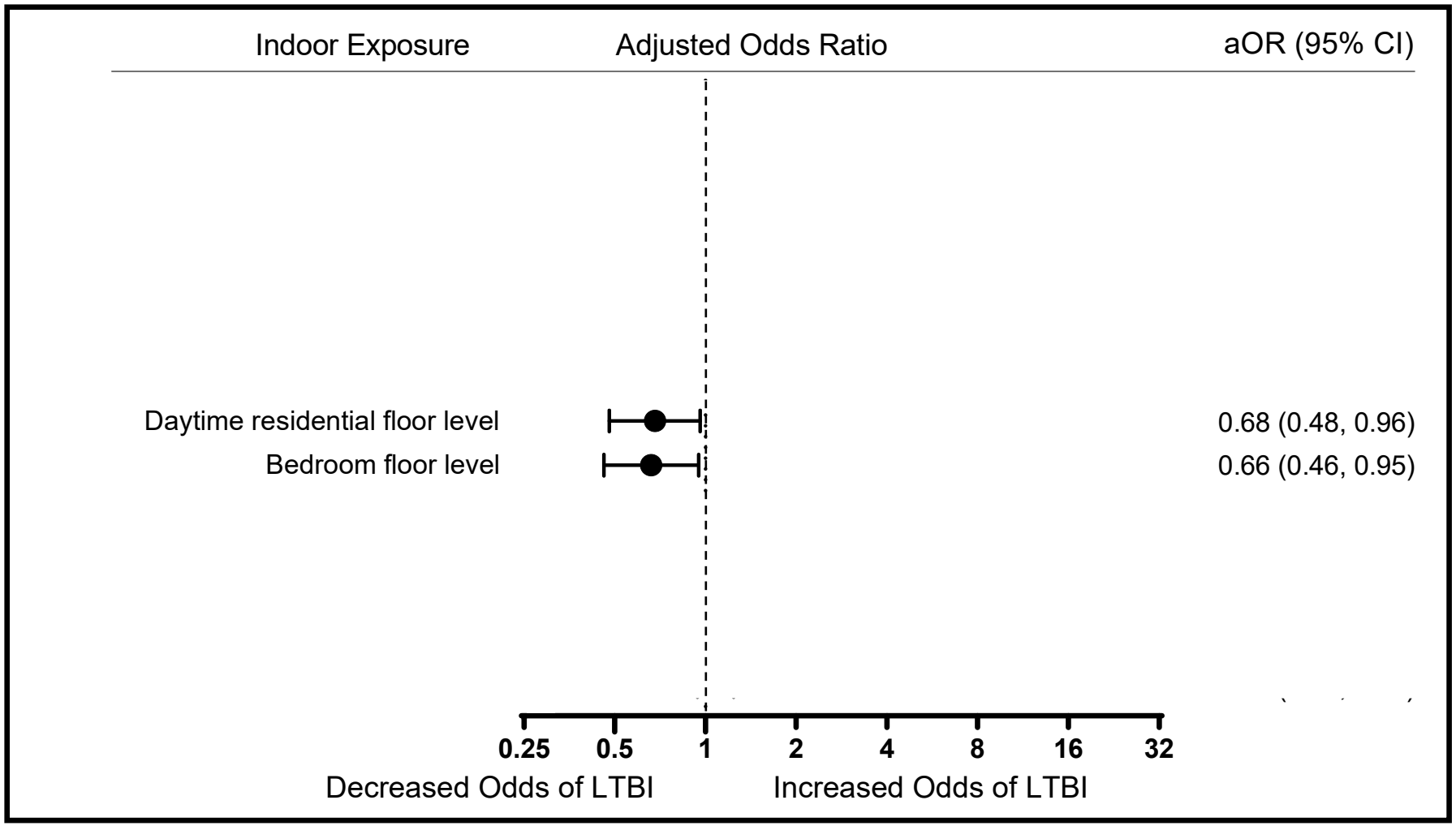
Blount & Nahid, AJRCCM 2021

Urban living in Vietnam

- In multilevel apartments
- On congested streets
- 95% of outdoor air pollution from motorcycles
- Living higher off the street: further from the pollution source

Hien, Sci Total Environ 2020
Chen, Atmosphere 2020

Higher floor levels decrease odds of infection



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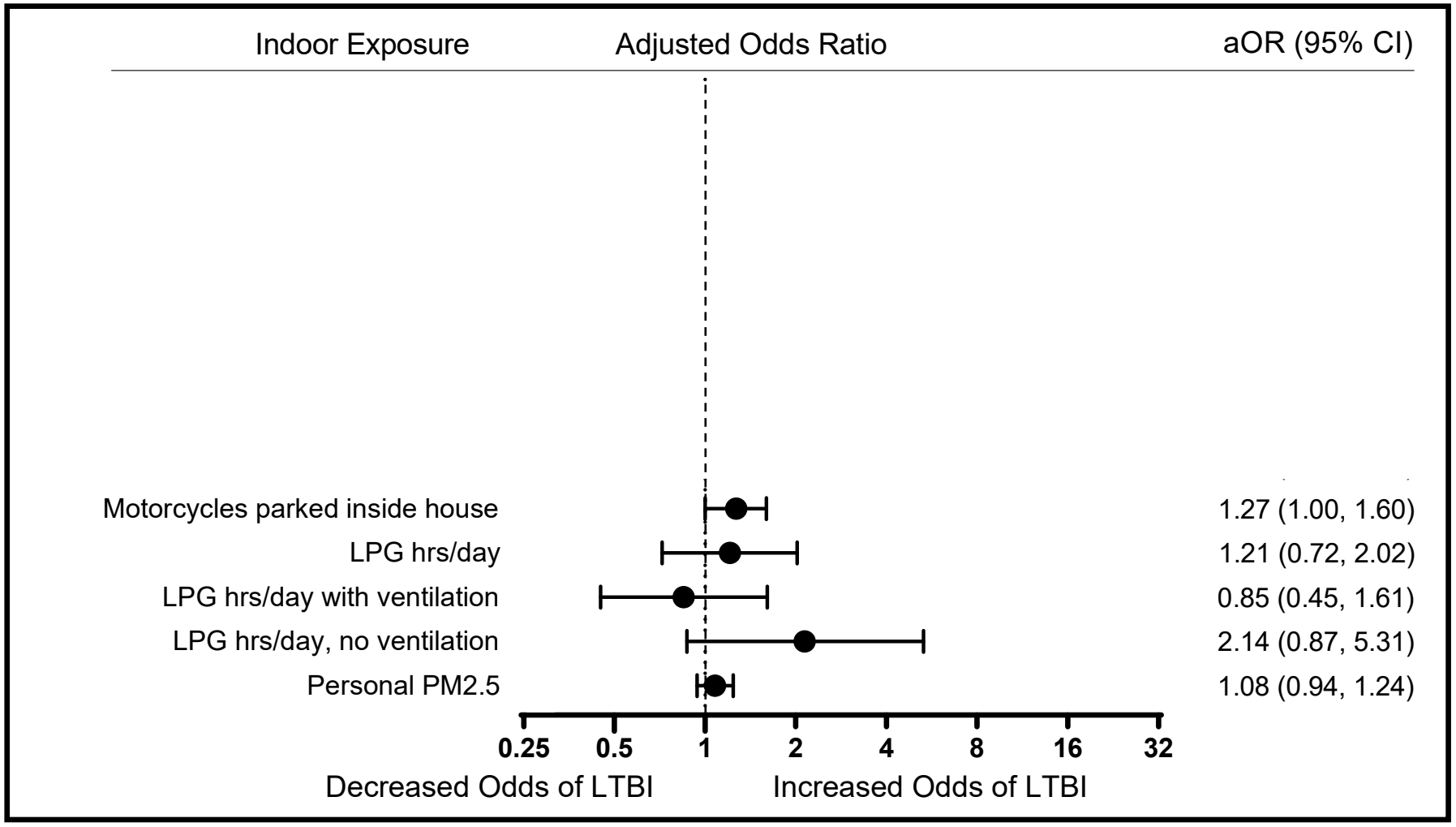
Motorcycles everywhere: even in the living room!

- Most people drive motorcycles
- No garages
- Evaporative emissions

Li, Sci Total Environ 2015

Indoor motorcycles increase odds of TB infection



Indoor motorcycles increase odds of TB infection

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Summary

- Smoking increases infection
- Vertical distance from street decreases infection
- Motorcycles parked in the home increase infection

Next steps

- Confirm findings in larger cohorts, other settings
- Real-time monitoring of indoor air pollution
  - Correlate with questionnaire responses
  - Confirm associations with TB infection
- Smoking cessation intervention in patients with active TB
  - Will TB patients stop smoking?
  - Will intervention decrease indoor air pollution?
  - Will intervention decrease TB infection?
- Motorcycle emissions reduction:
  - Natural experiment
    - Hanoi to ban motorcycle traffic after 2025.
    - Monitor household TB transmission before and after the ban.
  - Electric scooter intervention
- Indoor filtration intervention
  - Reduced air pollution
  - Reduced ambient Mtb from index case

Hypotheses

Southeast Asian urban indoor air pollutants:

1. Increase TB infection among child household contacts of active TB patients

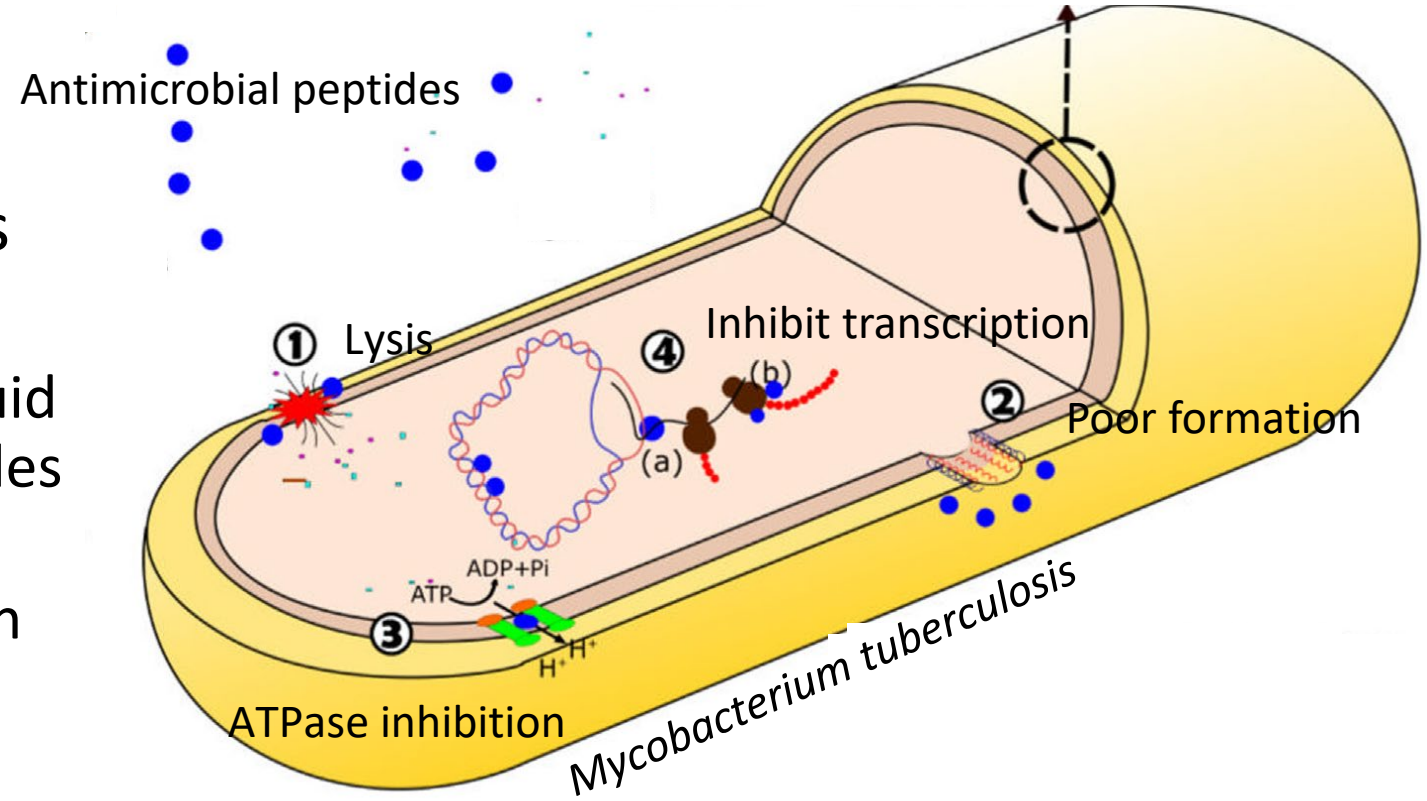
2. Decrease innate immune responses to Mycobacterium tuberculosis

Air pollution & Innate Mechanisms Against TB infection

- Mucocilliary transport — *Thomson, Nature 1971*
  - Inhibited by tobacco smoke
- Alveolar Macrophages (innate/adaptive) — *Rylance, AJRCCM 2015*
  - Fine particulate matter inhibits phagocytosis and T cell recruitment
- Airway epithelial cells — *Vargas, Environ Health Perspect 2017*
  - Does air pollution inhibit antimicrobial peptide activity against Mtb?
- Lung innate lymphocytes
  - Altered by air pollution?

Innate immune responses to TB

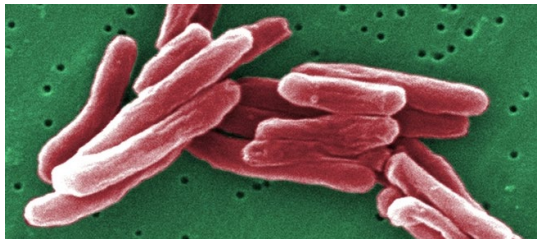
- Airway epithelial cell defenses
  - Mucociliary clearance
  - Secretion of airway surface liquid containing antimicrobial peptides → killing of bacilli
  - Tight junctions prevent invasion

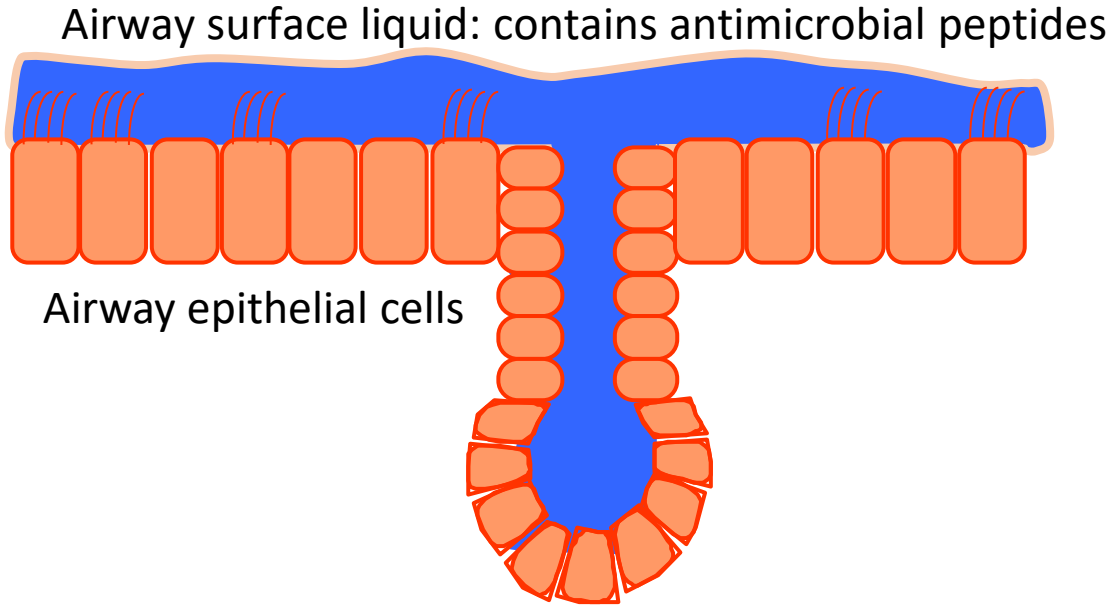


Arranz-Trullén, Front Immunol 2017

Can Airway Surface Liquid Kill *Mycobacterium*?

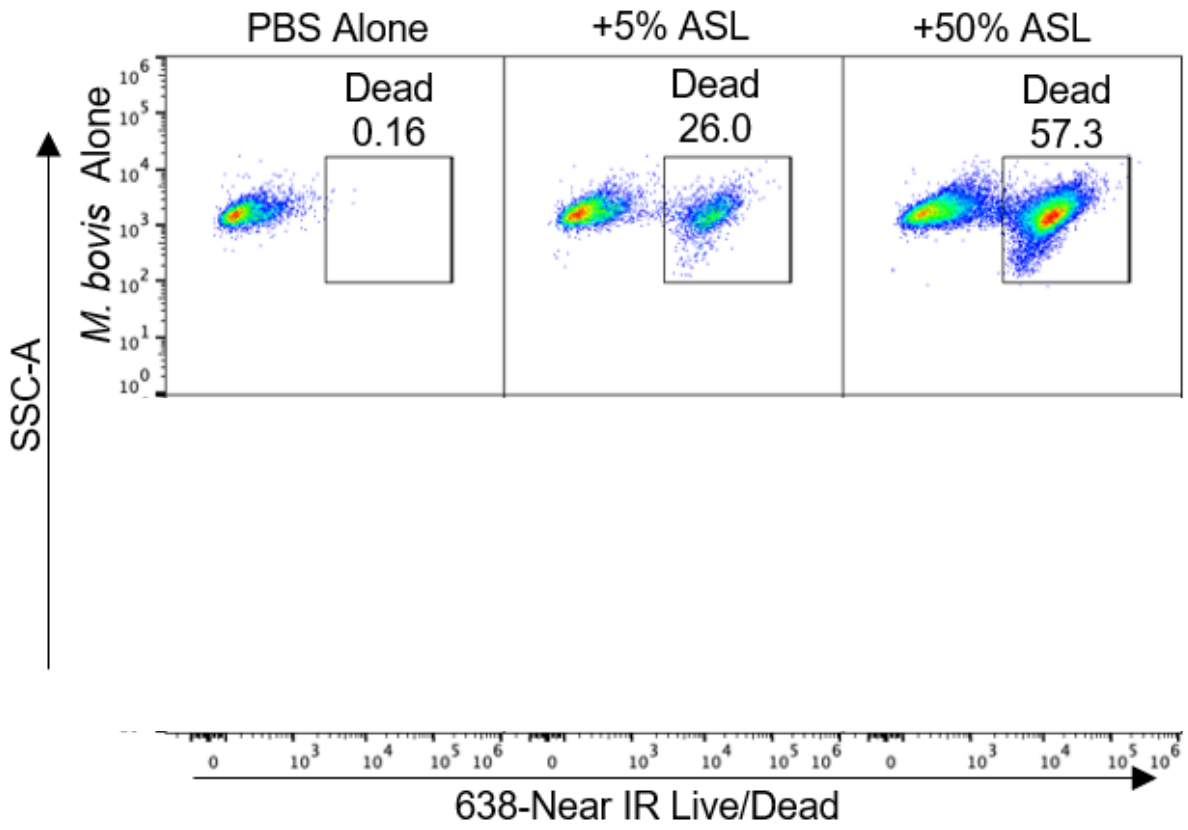
M. bovis



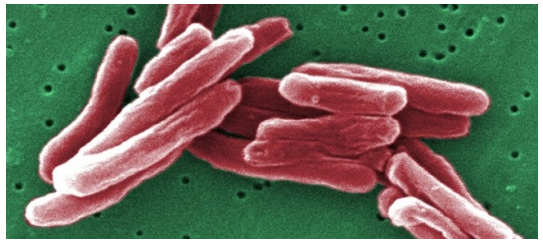


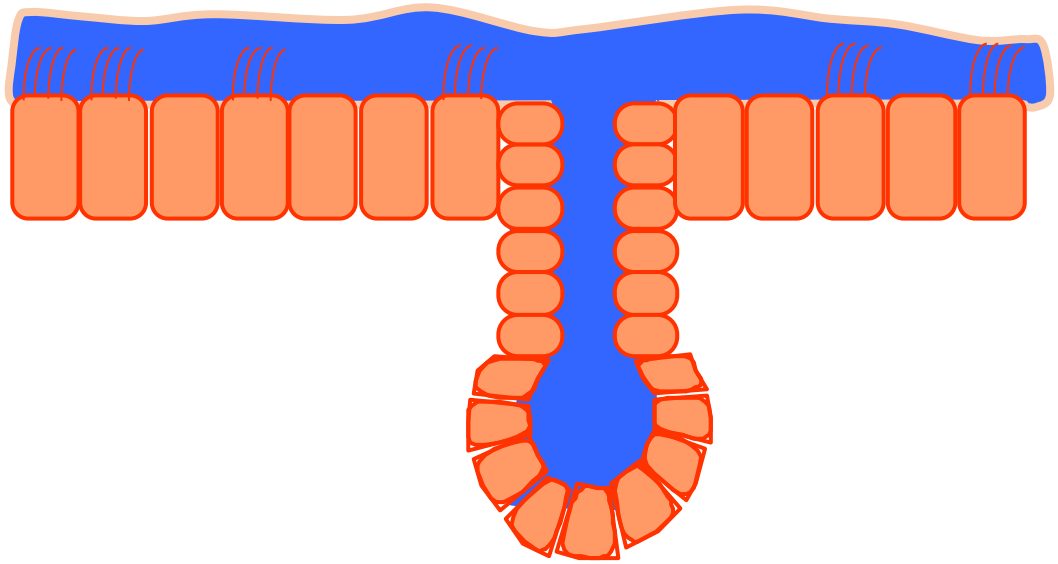
- *Mtb* requires BSL3
- Use attenuated *M. bovis (BCG)*
- Collect airway surface liquid(ASL) from cultured human airway epithelial cells
- Expose *M. bovis* to ASL for 5 min
- Count viable bacilli using flow cytometry

Airway Surface Liquid kills *M. bovis*



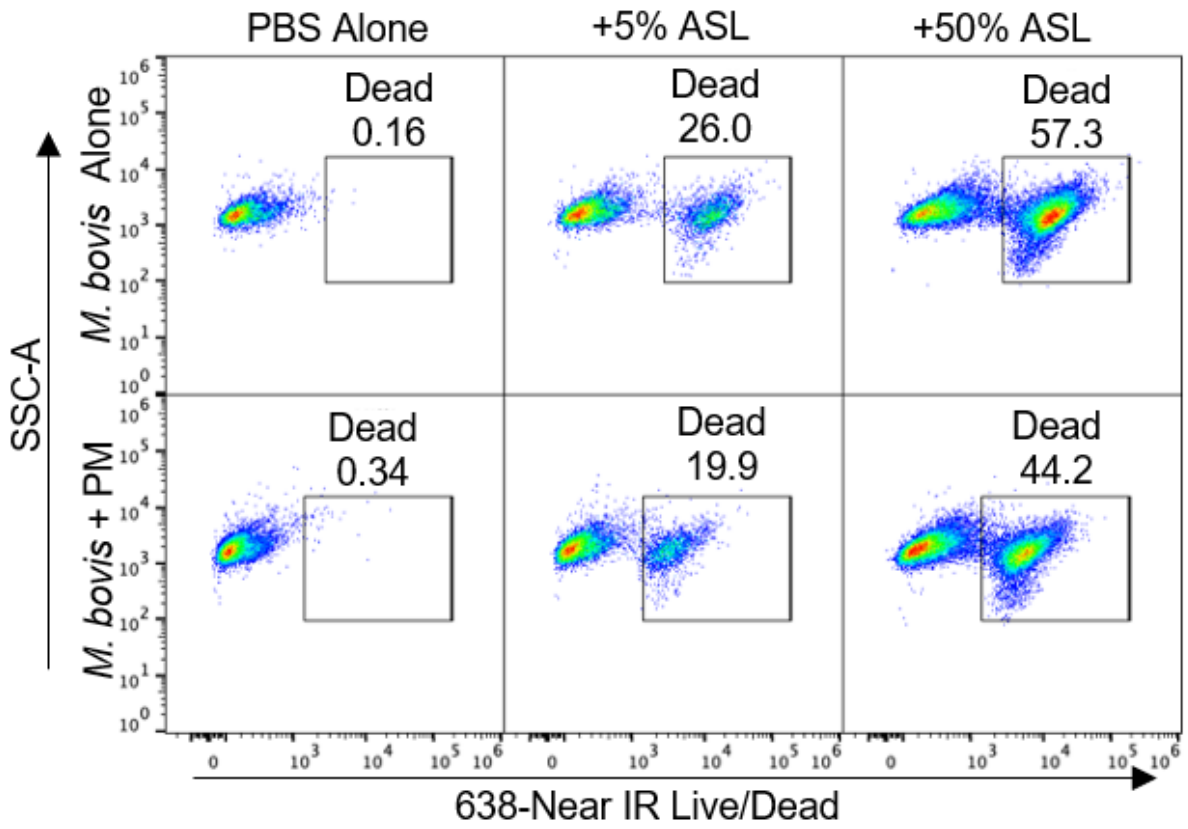
Does air pollution inhibit killing?



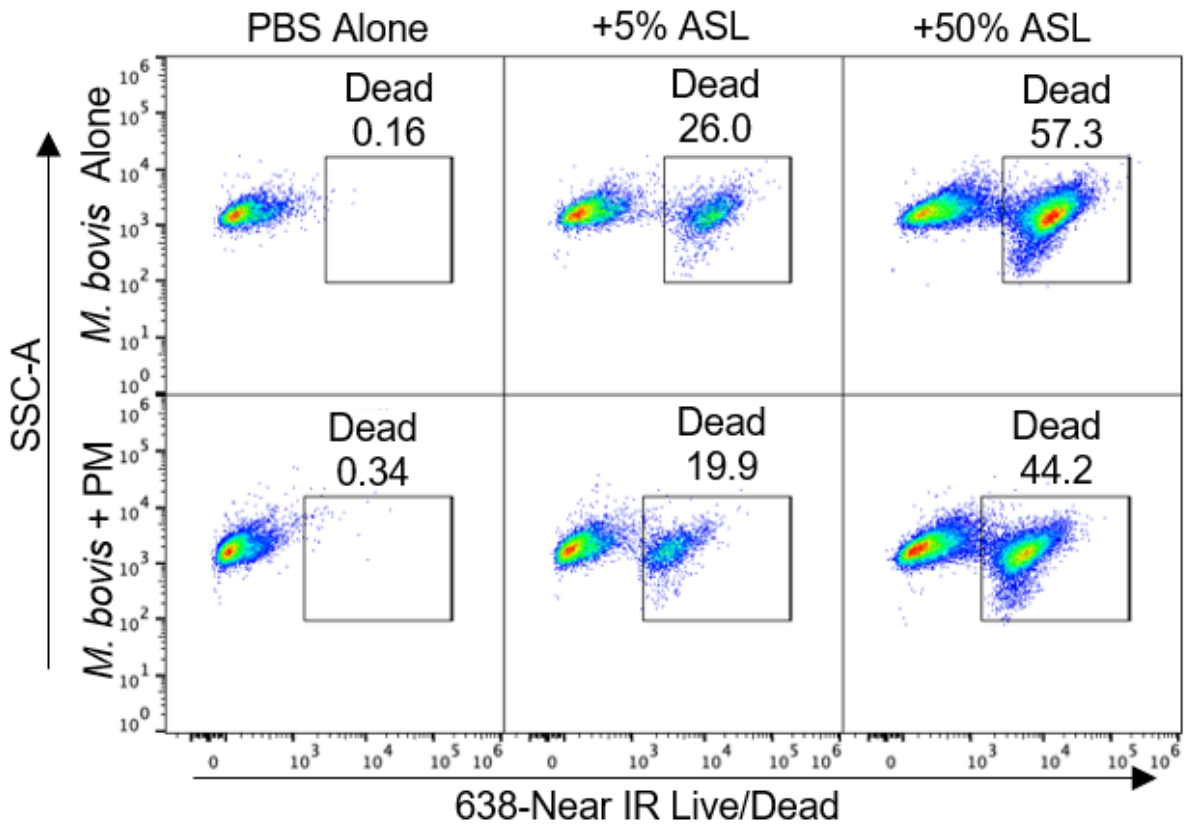


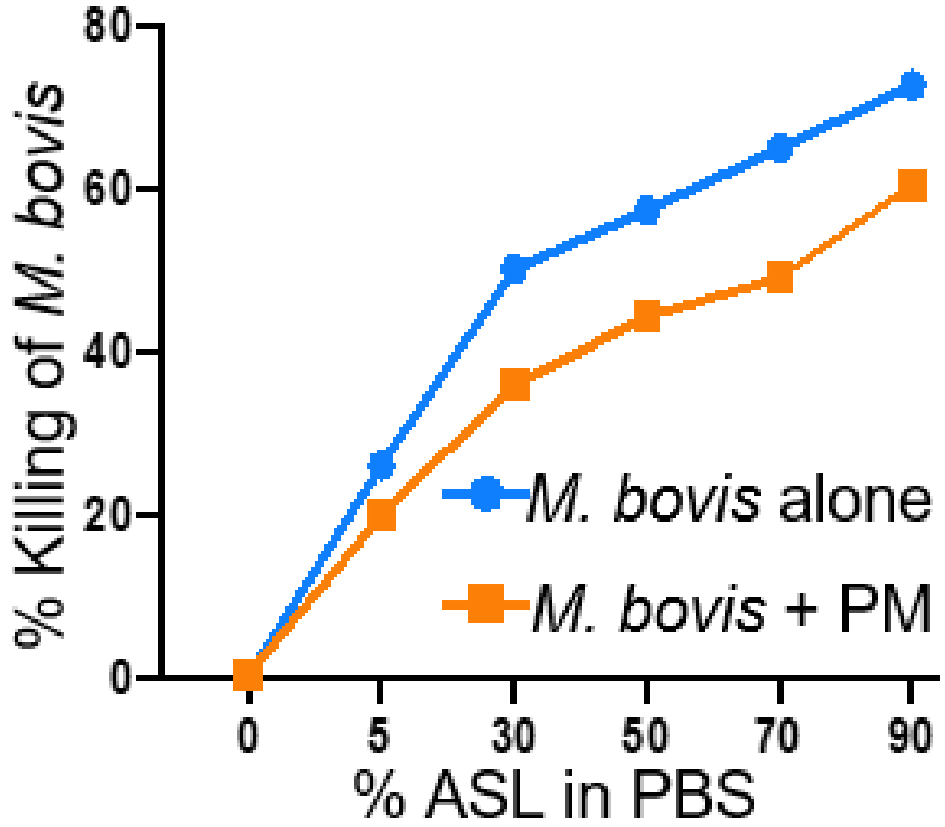
- Collect Hanoi air pollution particulate matter (PM) on filters
- Add PM to ASL
- Expose *M. bovis* to ASL and PM

Air Pollution Inhibits ASL Killing of *M. bovis*



Air Pollution Inhibits ASL Killing of M. bovis



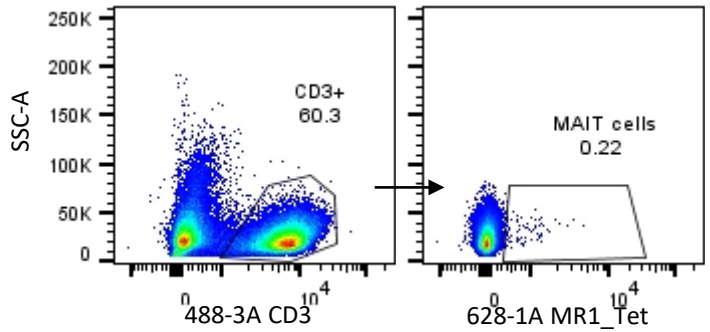


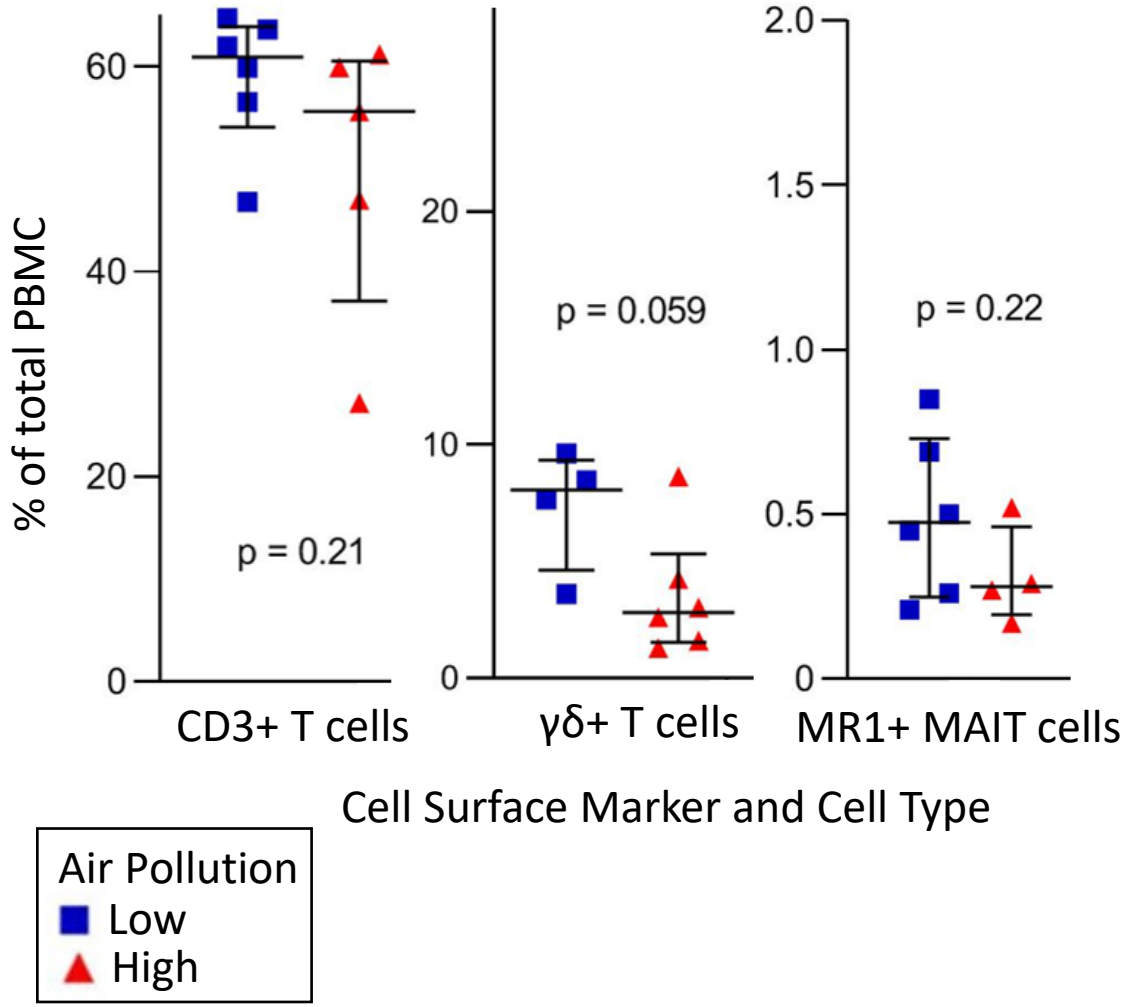
Innate lymphocyte responses to TB

- Traditional role of lymphocyte: adaptive immune system
- More recently characterized “innate” lymphocyte populations:
  - Innate immune function not requiring antigenic activation
  - Resident lung populations
  - Could play an early role against TB infection
  - Mucosal Associated Invariant T (MAIT) cells
  - Natural Killer T cells
  - γδ T cells
  - Innate Lymphoid Cells (ILCs)

Does Air Pollution Alter Innate Lymphocytes?

- Isolate peripheral blood mononuclear cells (PBMC)
- Cell surface staining
- Flow cytometry





Does Air Pollution Alter Innate Lymphocytes?

- Isolate peripheral blood mononuclear cells (PBMC)
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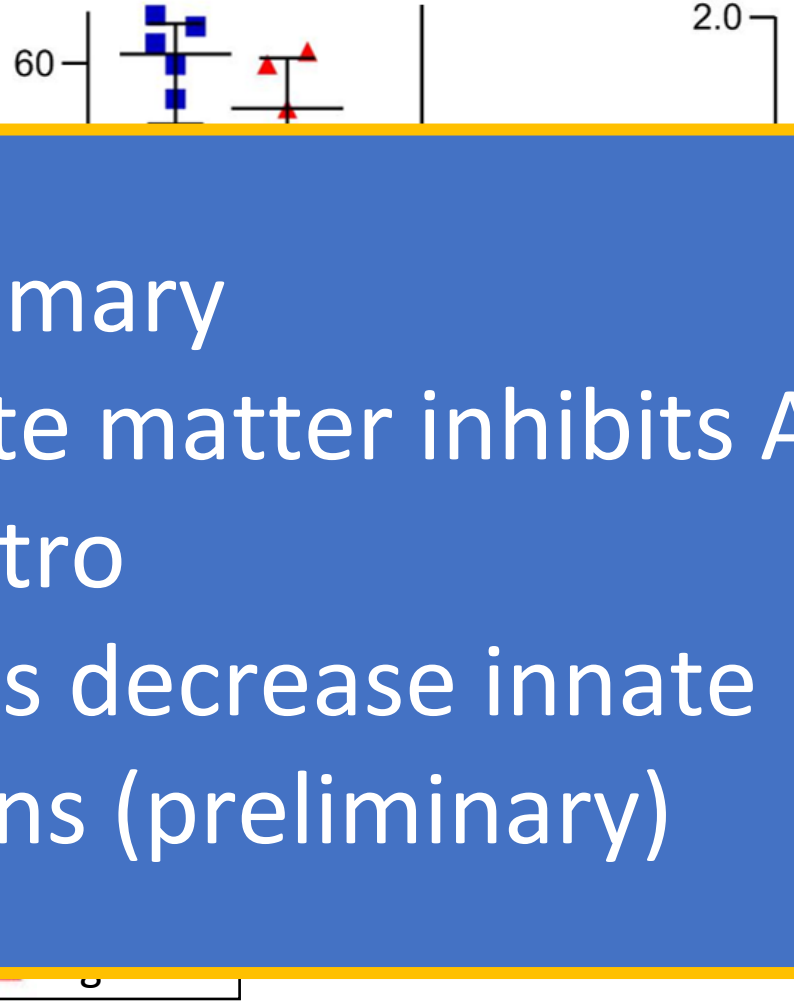

Summary

- Air pollution particulate matter inhibits ASL killing of *M. bovis* in vitro
- Air pollution exposures decrease innate lymphocyte populations (preliminary)

Overall Conclusions

- Indoor air pollutants (secondhand smoke, motorcycle emissions, street pollution) may increase susceptibility to TB infection
- Further Observational and Interventional studies needed to confirm findings
- Mechanisms through which air pollutants inhibit innate immune responses to TB need to be elucidated.

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